

# ANNALS OF SURGERY

VOL. 114

NOVEMBER, 1941

No. 5



## THE PROPHYLAXIS OF PULMONARY EMBOLISM BY DIVISION OF THE FEMORAL VEIN

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THE PURPOSE of this communication is to offer evidence that division of the femoral vein is advisable as a *routine* prophylactic measure against pulmonary embolism when thrombosis of the deep veins of the lower leg is present or suspected.\*

The common impression that a pulmonary embolus is an unavoidable accident is no longer tenable. Available evidence demonstrates that the site of origin of the thrombus responsible for the pulmonary embolus is, as a rule, not in such inaccessible areas as the iliac and pelvic veins, but rather in the veins below the common femoral and, primarily, in the veins below the knee. In 133 cases of venous thrombosis, Frykholm<sup>1</sup> by anatomic dissection found the following distribution: Eighty-five (64%) were located in the popliteal vein or its branches; four (3%) in the femoral vein distal to the vena profunda; 25 (18%) in the vena profunda or its branches; four (3%) in the common femoral; two (1.5%) in the iliac veins; and eight (6%) in the deep pelvic veins. It is, therefore, clear that in 85 per cent of Frykholm's cases of venous thrombosis the process was distal to the entrance of the profunda, *i.e.*, in the femoral vein and, primarily, in its branches below the knee.

Neuman,<sup>2</sup> in an unselected series of 165 patients, dead of a variety of diseases, surgical and otherwise, studied the veins of the leg by dissection of the plantar and thigh veins and by serial sections at 2 cm. intervals along the veins of the lower leg. Venous thrombosis was found in 100

\* It should be clear that we are not concerned in this paper with pulmonary embolism arising from auricular fibrillation or any vascular disorder of the venous system cephalad to the great veins in the pelvis.

cases; in 52 per cent the process was bilateral. Thrombosis in the veins of the thigh was present in 45 per cent, but in every instance only as a continuation of a more distal thrombosis and never as an isolated process—an observation recently confirmed in the living subject by Bauer.<sup>10</sup> Neuman demonstrated the segmental distribution of the thrombosis, with intervals of freedom at those points in the lower extremity where compression by extra-venous structures is likely. Thrombosis, solely in the plantar veins, was equally distributed among all decades from 20 to 80 years of age; thrombosis, solely in the deep veins of the calf, increased in frequency with age. Neuman considers thrombosis in the plantar veins a more malignant type because it gave evidence of a greater predisposition toward rapid propagation of the clot into the veins of the thigh. Twelve per cent of cases with thrombosis showed massive pulmonary emboli. An additional 34 per cent showed multiple nonfatal emboli.

Roesslé<sup>3</sup> found thrombosis in the deep veins of the calf in 88 of 324 routine autopsies in adults over 20 years of age. Of these, 38 showed, in addition, thrombosis in the femoral veins. Ten cases showed massive pulmonary emboli arising from the femoral vein, in all of which there was an associated thrombosis in the calf veins.

In a statistical study of 897 cases of fatal and nonfatal embolism by Barker, *et al.*,<sup>4</sup> 45 per cent were said to have shown no clinical or necropsy evidence of venous thrombosis. The absence of clinical evidence is notoriously unreliable because thrombosis is often not demonstrable by prevailing clinical methods. The absence of necropsy evidence cannot be accepted as proved, because the examination did not include a dissection of the veins in the lower thigh and lower leg.<sup>5</sup>

Of a total of 1,401 cases of postoperative thrombophlebitis reported by these authors, 1,199 (85.6%) were in the veins of the lower extremities. Of these, 502 were in the "short saphenous" (which we would interpret as intended to mean the deep veins in the calf), 160 were in the long saphenous, and some 537 in the iliofemoral veins. It is not possible to learn from the evidence given how many of the latter were extensions from the lower leg and how many were limited to the iliofemoral veins. In any case, since embolism from the long saphenous and from "primary" iliofemoral thrombophlebitis is rare,<sup>6</sup> it is clear from these data, also, that the parent source of most emboli is at a site below the common femoral.

On the basis of the above considerations the deep veins of the lower leg must be regarded, by far, the most common site of origin of venous thrombosis. The condition is dangerous because the thrombus frequently extends proximally as a long, soft clot, which, if detached, produces a fatal or nonfatal embolus, depending upon its size.

To anticipate such an accident is obviously preferable to the heroic type of interference described by Nystrom.<sup>7</sup> Intravenous heparin<sup>8</sup> seems effective, but it is not likely to become a universally adaptable method (1) be-

cause of its expense, and (2) because it involves too much of a burden on the patient to justify its routine employment in postoperative patients, even if limited to people of middle and advanced age. Since the preventive measures now in general use<sup>9</sup> are frequently unsuccessful, even when conscientiously applied, thrombosis continues to be an unsolved problem. In these circumstances, division of the femoral vein is the only promising alternative as an efficient prophylaxis against embolism. This procedure was first recommended and applied by Homans and has been so employed occasionally, by others.<sup>10, 11, 12</sup> Our purpose is to show why its adoption as a *routine* measure is essential if a significant reduction in the morbidity and mortality from embolism is to be achieved.

As stated at the beginning of this communication, the procedure should be utilized when thrombosis of the deep veins of the lower leg is *present or suspected*. Such a diagnosis requires careful and repeated examination of the lower legs for the earliest manifestations of this disease. These are (1) pain or tenderness in the sole of the foot or ankle, but usually in the calf muscles; (2) pain on forced dorsiflexion of the foot (Homan's sign<sup>9</sup>); (3) slight fever; (4) increased local heat (delayed cooling—Pilcher<sup>13</sup>); (5) local edema; (6) induration; (7) fulness of superficial veins; and (8) slight cyanosis.\* Unfortunately any or all of these signs and symptoms may be absent.

In the total absence of local evidence of thrombosis, the diagnosis of course cannot be made unless a pulmonary embolus discloses its presence. Fatal embolism may occur as a first event in the total absence of localizing signs or symptoms. Such unanticipated catastrophes cannot be avoided when the site of thrombosis is in such inaccessible areas as the pelvic or iliac veins. But since the large majority, as already indicated, arise in the deep veins of the lower leg, many fail of anticipation not because the thrombosis is clinically undemonstrable, but because a meticulous inspection of the lower legs in immobilized individuals, postoperative and otherwise, has not yet become a clinical habit.

Bauer<sup>10</sup> recently introduced a technic, similar to that described by Dougherty and Homans,<sup>18</sup> which is apparently effective for the adequate visualization of the deep veins of the lower extremity: A venogram, taken after 20 cc. of a 35 per cent solution of perabrodil† are slowly injected

\* The term "phlebitis" as used in the subsequent text, refers to this clinical syndrome, which is different, at least in degree, if not in type, from the condition commonly known as milk-leg—a far more outspoken syndrome, in which the process apparently centers in the iliofemoral veins and is accompanied by considerable fever and marked edema of the whole leg; but which is only rarely responsible for pulmonary embolus. Incidentally, the prevailing opinion that so-called primary iliofemoral thrombophlebitis arises, *ab initio*, in the iliofemoral veins is based on the fact that the clinical signs and symptoms are first noticed in the region of these veins. The accumulating evidence from adequate pathologic studies raises the suspicion that the process in many, if not most, instances is an extension from a silent thrombosis lower down.

† Diodrast is probably the best approximation on the American market.

into the small saphenous vein, exposed under local anesthesia, at the ankle (with the heel elevated on a 6 cm. block), will disclose the presence or absence of a deep phlebitis. The special virtue of this procedure is two-fold: (1) If a nonfatal embolus has occurred in the absence of local signs or symptoms of phlebitis, the side on which it exists can be determined; (2) by disclosing the extent of involvement of the femoral vein, a guide to the level for effective prophylactic division of the great veins in the groin is provided. Venography, immediately following the rapid injection of 20 cc. of a 50 per cent solution of perabrodil into the internal saphenous at the mid thigh, can be utilized to determine whether the process has progressed beyond this region.

A policy of routine division of the femoral vein, when thrombosis is discovered by local evidence or by the occurrence of a nonfatal embolus, can receive sympathetic consideration only if the risks of inaction can be shown to outweigh, by a good margin, the risks of intervention. The risks of inaction cannot be assessed with precision from existing statistical evidence because many cases of thrombosis and of embolism are frequently overlooked or wrongly diagnosed.<sup>14, 17</sup> However, an approximation to the facts is possible. Pilcher's<sup>13</sup> data shows that about one person in 20, who had clinically recognizable thrombosis, died later of embolism, and about one person in 12 who had a previous nonfatal embolus, died of a subsequent embolus. The evidence from the recent studies of Barker, *et al.*,<sup>4</sup> is even more striking: One person in 17 (30 out of 502 cases of thrombophlebitis in the "short saphenous"), who had clinically recognizable thrombosis in the deep veins of the lower leg, died later of embolism; one person in five or six with a previous nonfatal embolus (124 out of 678 cases of nonfatal embolus) died of a subsequent embolus. Barker, *et al.*, conclude that if all fatal embolisms which were preceded by a clinically diagnosed nonfatal embolism could be prevented, the total number of the fatal embolisms would be reduced by about one-third." In our view, the foregoing facts constitute a situation akin to any threatening emergency in which there is a substantial likelihood of a fatal complication.

To illustrate the disastrous consequence from failure to intervene when thrombosis in the deep veins of the lower leg is known to exist, we cite the following recent experiences:

**Case 1.**—An obese, hypertensive diabetic female, age 63, entered the hospital with a painful left great toe which showed signs of vascular insufficiency. For two years she had had signs and symptoms of peripheral vascular disease of both legs, and for five weeks, pain in the left leg while resting. After conservative measures failed to afford relief amputation was advised, but the patient insisted on relief of pain by a less radical method. Three of the sensory nerves to the foot were crushed, through appropriate incisions in the lower third of the leg, on the twentieth day of her hospital stay. The following day she complained of an unusual amount of pain in the calf of this leg, examination of which showed edema, slight cyanosis and venous engorgement. The temperature was 101° F. Because of the prevailing lack of a decisive policy as to whether or not to divide the femoral vein in phlebitis of the leg, decision was deferred.



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The next morning on getting into a chair she collapsed, became cyanotic and died suddenly with all the classic signs and symptoms of massive pulmonary embolus.

**Case 2.**—A male, age 43, was admitted for Buerger's disease of both lower extremities and hypertension. The deficiency in the circulation of the left leg was due more to vasospasm than to organic occlusion. Accordingly, a left lumbar sympathectomy was performed. Five days later there was slight hemoptysis, his temperature rose to 103° F., and he showed signs in the right lower lobe which were interpreted as due to an infarct, with superimposed pneumonitis. He was clinically cured of this complication by the twelfth postoperative day. But on the fifteenth postoperative day he complained of slight pain in both legs. There was tenderness on pressure over the calf muscles, and phlebitis was suspected. In this, as in the preceding instance, division of the femoral vein was under consideration but not carried out. Twenty-four hours later he was seized with substernal distress, became dyspneic and cyanotic, and died in less than ten minutes.

**Case 3.**—A male, age 69, walked into the hospital complaining of pain in the right lower quadrant of the abdomen of 36 hours' duration. There was vomiting at the onset of the illness, and he had had two severe chills on the day before entry. Until then he had always enjoyed good health. Physical examination showed a temperature of 104.5° F., pulse 90, respiration 20. The cardiorespiratory system was within normal limits. Except for a right hydrocele there was nothing else of note except evidence of a mass in the right lower quadrant which was presumably an appendiceal abscess. Under local infiltration anesthesia, an acutely inflamed appendix was removed. There was a large mass of inflamed mesentery around the appendix and evidence of local pyelephlebitis. The following day the temperature was normal and remained so. Because of his age and his apparent state of well-being, he was allowed out of bed. He sat up most of the day and walked during the last two of the subsequent six days, during which he felt entirely well. On the afternoon of the sixth postoperative day he complained for the first time of pain in the right calf. Examination showed moderate edema of the calf and ankle and tenderness on deep pressure over the calf muscles. He was put to bed with the intention of dividing the femoral vein the following morning, should no improvement in the phlebitis occur overnight. At 7 A.M. of the seventh day, after an entirely comfortable night, while talking to the nurse, he suddenly felt acute substernal distress, became dyspneic and pale, and died within a few minutes.

**COMMENT.**—In all three patients the existence of phlebitis in the lower leg was known in advance of the detachment of the embolus. The evidence for phlebitis was clear-cut in Cases 1 and 3, and suggestive in Case 2. A complacent attitude toward the phlebitis in the latter instance could hardly have been justified on the basis that the signs and symptoms were not outspoken. The first embolus was sufficient notice of its presence. The experience in all three patients demonstrates the fact that there is no period of watchful-waiting that may be considered a safe interval between the onset of phlebitis and the liberation of an embolus. Had a policy of intervention, by division of the femoral vein, instead of one of hesitation been adopted, there is good reason to believe that death could have been prevented.

The prophylactic effectiveness of division of the femoral vein cannot be proved in any given case in which it is undertaken, for no one can assume that, otherwise, an embolus would have been discharged from the area caudad to the division. Its value can be affirmed with certainty only after routine division in a very large series of patients with phlebitis should

succeed in demonstrating an incontrovertibly lowered incidence of pulmonary embolus, fatal or nonfatal. Nevertheless, the protective effect of dividing the femoral vein seems to have been demonstrated in the following illustrative cases:

**Case 4.**—A male, age 40, with well-marked thromboangiitis obliterans of the left leg, was submitted to denervation of the foot for relief of pain, by crushing the appropriate sensory nerves above the ankle, under spinal anesthesia. Five days later he complained of pain in the left calf. Fever, leukocytosis and edema of the leg were noted at the same time. That evening he complained of pain in the left anterior chest, aggravated by inspiration. On the sixth day there were dyspnea, cyanosis and signs of consolidation in the left lower lobe. The roentgenologist interpreted the film of the chest as showing "consolidation at the left base, probably a pneumonitis, possibly an infarct." On the seventh day the left femoral vein just below the profunda was divided. Hippuran was injected into the distal end of the vein, and the roentgenogram showed a cone-shaped filling defect. Slow resolution of the pulmonary process occurred and he seemed much improved on the sixteenth day. But on the eighteenth day he complained of pain in the right calf which was tender on pressure and there was slight pretibial edema. Fever recurred, and on the twenty-fourth day there was evidence of infarction in the right lower lobe. The right femoral vein was divided just below the profunda that evening. Two days later he complained of pain along the right femoral vein in Hunter's canal. Resolution of the phlebitis and the pulmonary infarction occurred, and he was discharged, well, 12 days after the second vein was divided.

**Case 5.**—A female, age 47, had a cholecystectomy, under nupercaine spinal anesthesia. Nine days later she felt some pain in the right calf but did not mention it to the house officer. On the eleventh postoperative day she was allowed to sit up with the feet over the bedside. That afternoon she was dyspneic and felt "a heaviness over the breast bone, like a cold coming on." The temperature rose, the pulse increased to 130, and respirations to 30; but all of these signs and symptoms subsided the following morning. That afternoon she went into collapse, the blood pressure fell to 45/30, there was dyspnea, cyanosis, sphincter incontinence, cold, clammy extremities, and a rapid thready pulse. The next morning there was tenderness in the right calf and the patient then admitted pain in this region during the preceding four days. A roentgenogram showed an infarct in the right lower lobe. Under local anesthesia, the right femoral vein was divided. After division the distal segment collapsed, suggesting a block to the flow distally. She was discharged, cured, 12 days later.

**Case 6.**—A female, age 54, complained of sudden pain in the right chest on the third day following the repair of a large incisional hernia. Fever, tachypnea, and signs of consolidation in the right upper lobe were noted the next day. A roentgenogram showed an area of increased density in the right upper lobe, which was interpreted as atelectasis by the radiologist. The right leg was swollen, and there was some pain deep in the adductor muscles of the thigh. Two days later the right femoral vein was divided. Roentgenography of the vein, after hippuran had been injected distally, showed a definite mottled filling defect, consistent with a large thrombus at the midportion of the vein, about 7 cm. long. The signs in the lung persisted for another week and then disappeared.

**Case 7.**—A male, age 65, with a carcinoma of the rectosigmoid, showed signs of pneumonitis at the right base 16 days following a cecostomy for acute obstruction of the colon. A roentgenogram was interpreted as showing "atelectasis, or perhaps an infarct." There was pain in the right chest but no evidence of phlebitis in either leg. Two days later the left leg was slightly swollen at the knee, but there was still no other evidence of phlebitis in either leg. Four days later there was much bloody sputum. Both legs were now swollen. Eleven days later pain in the right chest recurred, and there was marked hemoptysis. After a three-day interval, free from symptoms, he complained of

pain in the left calf. The same day both femoral veins were divided, with subsequent rapid disappearance of all signs and symptoms in the chest.

COMMENT.—In this patient an infarct was the first evidence of phlebitis. The appearance of bilateral swelling, along with further embolism, and finally pain in the left calf, led to bilateral division of the femoral veins with the desired result and without untoward sequelae. Intervention following the occurrence of the first infarct would have necessitated bilateral ligation and division because of the total absence of localizing evidence of phlebitis. Division of the femoral vein on an obviously involved side, as a matter of fact, will not guarantee protection against further embolism, for there may be a silent phlebitis on the opposite side. In this connection, the frequency with which Neuman<sup>2</sup> found bilateral thrombosis (52%) by anatomic dissection must be borne in mind. Since the radiologic diagnosis of phlebitis, not otherwise recognizable, is now possible,<sup>10</sup> hesitation to intervene when a nonfatal embolus has occurred can no longer be justified on the ground that a guide to the site of the phlebitis is lacking. In the present controversial phase of the problem, however, one may be content with unilateral ligation if there is an obviously involved side.

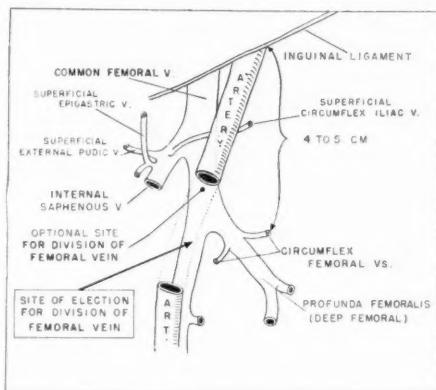


FIG. 1.—The anatomy of the region involved in division of the femoral vein.

Division of the femoral vein just below the vena profunda is the most desirable site for blocking the discharge of an embolus from the deep veins of the lower leg, because no proximal segment of vein with a sluggish stream is left, while the profunda and the internal saphenous remain as adequate pathways for the return flow of blood. The operative exposure necessary for this purpose (Fig. 1) permits a simultaneous examination of the vena profunda and a division of this tributary if it contains a thrombus or clot or if there is preoperative evidence of thrombosis in the deep tissues of the thigh (18 per cent in Frykholm's series). If division of the common femoral is necessary in order to shut off the profunda as well as the femoral, it may be done. A slight amount of transitory edema due to the division itself may result. Division of the femoral vein does not affect the phlebotic process adversely; on the contrary, the signs and symptoms generally subside rather more promptly than otherwise. This is evidently due to the fact that division of the vein simultaneously divides some of the sympathetic pathways involved in the reflex vasospasm, which not infrequently adds to the pain and edema attributable to the phlebitis.

If there has been much delay in the division of the femoral vein and

the soft clot has advanced beyond the common femoral, it can be sucked out. One may, however, find instead a firmly fixed thrombus, as in the following cases:

**Case 8.**—A male, age 70, was allowed to sit up on the ninth day following the repair of an incarcerated inguinal hernia. The next day he complained of pain in the right calf. There was deep tenderness over the calf and pain on passive dorsiflexion of the foot, but no swelling or fever. Division of the femoral vein was advised but refused. Three days later fever occurred, but the calf pain and tenderness had disappeared, while tenderness appeared in the femoral triangle. Division was again advised and this time accepted. The vein was found thrombosed and surrounded by an organizing exudate. A section of the vein was removed and showed beginning organization of a thrombus. Forty-eight hours later the temperature was normal, and the patient was discharged 96 hours after division.

**Case 9.**—A male, age 48, complained of pain in the right lower leg on the fifth day following a laminectomy for the removal of a ruptured intervertebral disk. Examination of the leg showed mottled cyanosis of the ankle and edema and tenderness over the calf muscles. Early on the sixth postoperative day he suddenly went into collapse, became cyanotic and complained of pain in the lower left chest which was aggravated by inspiration. An electrocardiogram showed no changes suggestive of coronary occlusion. A roentgenogram on the seventh postoperative day was interpreted as showing an infarct at the left base. There was gradual improvement in the phlebitis and the pulmonary complication until the sixteenth postoperative day when he developed dyspnea and severe pleurodynia in the right axilla. A roentgenogram showed right pleural effusion and a probable underlying infarct. At this time edema of the right thigh was observed. The right femoral vein was then divided, but thrombosis extending above the inguinal ligament was noted. An excised segment of vein showed an organizing thrombus with perivascular edema and inflammation. Edema of the right ankle persisted for a month thereafter, and toward the end of this period edema of the left ankle was present.

**COMMENT.**—It is difficult to be certain that the right femoral vein was the source of both emboli. That it may possibly have been the left is suggested by the appearance of edema in the left leg at a late stage in the convalescence. There was an interval of 17 days between the onset of phlebitis in the right calf and the division of the right femoral vein. During the interval two successive infarctions occurred. The advancing thrombosis had by this time extended beyond the site of election for dividing the vein. This case illustrates the fact that the thrombosis does not always remain a localized process, with a superimposed soft clot. Waiting may allow the thrombotic process to advance beyond the point where division at the level herein recommended can be useful.

The indications for division in these circumstances have not as yet been clearly defined.<sup>15</sup> It is generally true that if the process extends proximally as a fixed thrombus, instead of as a clot, the danger of embolus is distinctly lessened. However, occasionally embolization will occur. This is well illustrated in the following case, although the thrombus in this instance involved the long saphenous rather than the deep femoral.

**Case 10.**—A female, age 69, entered the hospital, with acute intestinal obstruction. At the same time acute thrombophlebitis involving the entire right varicose saphenous vein was noted. A Miller-Abbott tube achieved satisfactory deflation of the intestine

within 48 hours. After four more days of restorative therapy, during which the right leg had been kept elevated, without significant change in the thrombophlebitis, she was prepared for exploration for carcinoma of the colon. While in position for nupercaine spinal anesthesia, with the legs firmly flexed on the abdomen, her respirations became rapid and shallow and the blood pressure fell to 60 systolic after 10 cc. of 1:1,500 nupercaine had been injected. Two doses of intravenous neosynephrin were given, the anesthesiologist expecting that she would shortly respond to the vasopressor treatment. Death followed shortly thereafter, and was attributed to nupercaine poisoning. Autopsy revealed an obstructing carcinoma of the cecum, with hepatic metastases, and a large, fresh embolus plugging the pulmonary conus. The embolus was shown to have arisen from the thrombus in the saphenous vein from which it broke off probably during the spinal anesthesia.

**COMMENT.**—The danger of a pulmonary embolus from saphenous thrombophlebitis is regarded as inconsequential. If manipulations of a patient can detach a presumably firmly fixed thrombus, the relative ease with which a patient's own movements or the manipulations of an attendant can dislodge a soft propagating clot in the deep system is obvious.

Division of the popliteal instead of the femoral vein is not satisfactory, as the following experiences show:

**Case 11.**—A female, age 70, complained of severe constant pain in the right calf and ankle 12 days after a left radical mastectomy for carcinoma of the breast. Marked edema, venous engorgement, slight cyanosis along the lower half of the right tibia and exquisite tenderness on pressure over the right calf were noted. Ligation (without division) of the right popliteal vein was performed immediately. No clot or thrombus was observed in this vessel. Ten days later there were signs and symptoms of a pulmonary infarct in the right lower lobe, confirmed by a roentgenogram of the chest. At the same time tenderness appeared along Hunter's canal, suggesting a new thrombus proximal to the site of ligation. Division of the femoral vein was advised but refused. The intensity of pain in the lower leg was much greater after than before ligation of the popliteal vein. The pain, edema and cyanosis were increased by the ligation, perhaps because the obstruction to venous return was too extensive. Mild edema of the leg was still present eight weeks later.

**Case 12.**—A male, age 52, 12 days after the repair of a recurrent left indirect inguinal hernia, experienced pain in the right calf muscles especially on dorsiflexion of the foot. There was no edema or cyanosis. Two days later the popliteal vein was divided. Following division the pain increased in intensity; fever occurred and edema appeared. The pain subsided somewhat after ten days, but he was not entirely free of pain three months after discharge from the hospital. Six months later he still had edema.

**COMMENT.**—Division of the popliteal vein should be avoided not only because it seems to aggravate the symptoms and prolong the morbidity, but also for the following reasons: (1) The thrombus or clot in the deep veins may be found extending beyond the popliteal. (2) Since the femoral vein below the profunda receives few branches of any consequence, division of the popliteal results in a sluggish column of blood which may permit the formation of a clot of sufficient length, if detached, to plug a large branch of the pulmonary artery.

A consideration of the risks involved in division of the femoral vein must take account of the possibility of initiating a thrombosis proximal to the site



of division. Since division just below or above the profunda does not leave a long proximal segment of vein lacking large active tributaries, there is no good reason to fear this possibility. In any case, there is no evidence of its occurrence in our experience, and no mention of it is made in the experience of Homans,<sup>15</sup> Faxon,<sup>16</sup> and O'Neil<sup>16</sup> when the vein at the site of division was free of clot or thrombus.

The risks involved must also take account of the possible undesirable late sequelae of the procedure, namely persistent edema, pain or functional disability. Such sequelae do not justify the conclusion that the division *per se* is any more responsible for them than the phlebitis for which the division was done. We cannot find, in our experience, that division below or above the profunda contributes, in any substantial degree, to what might have been expected had nothing been done. Indeed, as Homans<sup>9</sup> and Bauer<sup>10</sup> have repeatedly observed, the process was commonly observed to subside more quickly than otherwise as a direct consequence of the operation.

In a follow-up study, two to 20 months after discharge from the hospital, all patients with phlebitis, whether the femoral vein was divided or not, showed varying degrees of edema of the leg. In a few instances the edema was so slight that a woven bandage was not required. In the majority, the swelling, though moderate, could be controlled easily with appropriate support; without support the swelling at the end of the day caused heaviness and discomfort. Swelling was most marked in two patients in whom femoral vein exploration revealed extension of an organized thrombus beyond that level. Apparently the higher the obstructing thrombophlebitis, the greater the swelling when the patient becomes ambulatory, regardless of whether or not the vein has been ligated.

In several patients who were ambulatory before the diagnosis of thrombosis was made, no increase in swelling was observed after the femoral vein was divided. None of those who were operated upon developed, during the follow-up period, a degree of edema even remotely resembling that seen in "milk-leg." None gave evidence of postphlebotic induration or ulceration.

Efforts to locate the thrombus by roentgenographic visualization of the veins distal to the point of division during operation have yielded only occasional positive results. There were two patients in whom a filling defect indicative of a clot or thrombus was clearly demonstrated. In others the retrograde current of radiopaque medium was abruptly halted by valves or obscured by excessive dilution. This is to be expected in most instances because the radiopaque medium is injected usually at a considerable distance from the thrombus. Preoperative venography by the technic of Bauer<sup>10</sup> promises to render other methods obsolete.<sup>19</sup>

Since Hampton and Castleman,<sup>14</sup> Neuman,<sup>2</sup> and others<sup>17</sup> have demonstrated in autopsy material a high incidence of pulmonary emboli in non-surgical patients (without cardiac disease), the problem of pulmonary embolism from deep phlebitis can no longer remain the exclusive concern of the surgeon. The tendency to the development of venous thrombosis, a

necessary precursor of embolism, must be regarded as common to adults, especially over the age of forty, confined to bed, whether at home or in a hospital.

SUMMARY AND CONCLUSIONS

Thrombosis of the deep veins of the lower leg is the focus of origin of the great majority of pulmonary emboli.

Pulmonary embolism until recently has been regarded as a dramatic post-operative catastrophe for which adequate prophylactic or therapeutic measures are not available. This is no longer tenable except in the case of massive embolus which has occurred in the absence of detectable signs of venous thrombosis of the lower leg and in the absence of a previous episode of embolism.

If the surgeon will conscientiously observe the patient from the very beginning and throughout the postoperative period for the signs and symptoms of phlebitis in the deep veins of the lower leg, he is likely to discover the existence of at least suspicious evidence of phlebitis in a much larger number of instances than heretofore in advance of the discharge of an embolus.

If the evidence of phlebitis in the lower leg is clear-cut, immediate division of the femoral vein below or above the profunda should be done (bilaterally if both legs are involved). If embolism has not yet occurred, the procedure may be considered a justifiable prophylactic measure. If an embolus has been discharged, however massive it may be, so long as it is not fatal, immediate division of the femoral vein is the one most effective measure remaining to prevent the discharge from its commonest source of still another embolus which may prove fatal.

If the evidence of phlebitis is only presumptive, a decision can be reached by the venographic technic of Bauer.

If embolism has occurred in the total absence of signs or symptoms of phlebitis, the process will usually be demonstrated and lateralized by the venographic technic of Bauer. An embolus henceforth can be assumed to have arisen from the pelvic or other inaccessible veins only when no involvement of the deep veins of either lower extremity is shown to exist by employment of this technic.

There is no good evidence that division of the femoral vein involves any significant immediate risk or adds to the disability created by the phlebitis itself. On the contrary, aside from its prophylactic value for embolism, division appears to exert a favorable influence on the course of the disease probably because of the concomitant disruption of some of the pathways involved in the accompanying vasospastic reflexes.

Because pulmonary infarcts and fatal pulmonary embolism due to phlebitis of the lower leg occur frequently in nonsurgical as well as surgical patients, the therapeutic problems involved become the common concern of the internist as well as the surgeon.

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# THE MANAGEMENT OF LYMPH NODES IN THE NECK— METASTATIC FROM CARCINOMA OF THE MOUTH\*

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It is generally conceded that cancer is a local lesion at first; that there is no means of determining how soon metastasis may take place, or whether it has taken place, until considerable progress in the secondary growth has occurred; that removal of the local lesion only is useless if metastasis, whether recognizable or not, has taken place. Nevertheless a large volume of literature exists arguing against the value of lymph node excisions in intra-oral cancer.

The local lesion in buccal carcinoma is rarely the cause of death. Metastatic involvement of the cervical nodes, with its sequelae, is the usual cause. Treatment of the cervical drainage area may be by disregard, by radiation, by surgery, or by a combination of the latter two. A defeatist attitude toward the ultimate result of any type of treatment of any carcinoma is still all too common among the lay public, the general medical profession, the general surgeon, and the general radiologist. This is one of the reasons why treatment, recommended by surgeons or radiologists specializing in the cancer field, is often carried out in an indifferent fashion by others. The motions of giving treatment are gone through, but, evidently with no expectation of permanent good result. The mortality from buccal carcinoma is shown in Table I.

TABLE I  
CANCER OF THE BUCCAL REGION (NOT INCLUDING PHARYNX)  
IN UNITED STATES REGISTRATION AREA

	Deaths		Per 100,000	
	1914	1935	1914	1935
Cancer of:				
Lip.....	376	727	0.6	0.6
Tongue.....	614	1,076	0.9	0.8
Mouth.....	230	550	0.3	0.4
Jaw.....	851	999	1.3	0.8
Others.....	199	600	0.3	0.5
Totals.....	2,270	3,952	3.4	3.1

Since 1914, the advent of external radiation and interstitial radium has added a powerful weapon to cancer treatment in many locations. In the early years its use was in the experimental stage and statistics could not be considered of permanent value. For several years past many of its advocates have been sufficiently satisfied with their results to advise against the use of surgery

\* Read before the Third International Cancer Congress, Atlantic City, N. J., September 14, 1939.

in some locations. One of these is the routine dissection of lymph nodes in the neck—metastatic from carcinoma of the mouth.

Block dissections of the neck were never a popular operation with the general surgeon. It is a field in which he is not called on to work frequently. The procedure is a prolonged one requiring patience, meticulousness, and an enthusiasm about the ultimate result. An intimate knowledge of the anatomy of the neck is required. For these various reasons, block dissections of the neck have been in many instances a name only, rather than a true description of the method which was carried out. Therefore, the general surgeon was often pleased to side-step these procedures, when he found that a radiotherapist would take them off his hands.

Here is one of the most obvious lesions, causing early symptoms, not requiring any complicated aids to diagnosis, which should have been affected by lay education at least as much as any other lesion. The local lesion can be eradicated by either radiation or surgery, and this must always be done before operation on the lymphatic drainage area which is affected. I believe the local treatment usually has been rendered well for some years past. But it is the metastatic involvement which generally kills. Block dissections of the neck seem to be performed less frequently and, in spite of radiotherapy, the death rate has improved but little over a period of 21 years. It can be arranged from this that the lymph node problem is not being handled vigorously enough.

Except in the radio-sensitive Grade III and IV lesions, there is little definite evidence that external radiation has a permanent arresting effect on squamous carcinoma—metastatic to the cervical nodes. Neck surgery should not be undertaken in Grade III and IV lesions or in lymph-epithelioma. Complete regression of epidermoid carcinoma, metastatic in cervical nodes, from external radiation alone has been reported by some authors. Since an inflammatory node can be mistaken readily for a metastatic node, these results must always remain inconclusive. Many of the most experienced radiologists do not agree that this complete regression occurs. Possibly by most radical irradiation this could be obtained, but I have not known of this being administered except in advanced metastases. Most radiologists claim few, if any, five-year arrests with pathologically proven involved nodes.

It is commonly argued that prophylactic neck dissections, *i.e.*, when lymph nodes are not palpable or, being palpable, are believed not to be involved, is unnecessary surgery, since often the pathologist fails to find any involvement. This does not necessarily mean that no metastasis to the region excised has occurred. The pathologist has not *found* carcinoma in any of the sections which he examined. Naturally, he does not make serial sections of all the tissue sent to him, but of nodes or regions which appear suspicious to him. It is possible, theoretically at least, for one or a few metastatic cells to be present in a regional lymph node and impracticable for the pathologist to find them. Without a prophylactic neck dissection such deposits may continue to grow.



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In a series of 64 patients with carcinoma of the lower lip, in whom no lymph nodes were felt and in whom prophylactic neck dissections were performed, we<sup>1</sup> found metastases in nine instances, or 14 per cent. Simmons and Daland<sup>2</sup> reported similar findings in 25 per cent. Morrow,<sup>3</sup> of our institution, found that of 18 tongue cases, in which it was stated that no nodes were palpable and prophylactic neck dissections were performed, metastases were present in seven instances, or 39 per cent. Phillips,<sup>4</sup> in 31 cases of buccal carcinoma with no clinical metastases, found microscopic involvement in 16, or 51.6 per cent. Simmons,<sup>5</sup> in 20 cases of oral carcinoma with non-palpable nodes, found seven which proved to be cancerous, or 34 per cent. We do not grant that lack of palpable nodes in the neck means that metastasis has not occurred.

Among 98 patients in our series<sup>1</sup> with carcinoma of the lower lip in whom lymph nodes were felt and neck dissections were performed, tissue examination proved that metastases were present in 32 instances, or 33 per cent, and the remaining cases showed hyperplasia only. Regaud<sup>6</sup> states that palpable nodes are cancerous in 60 per cent of these cases. Morrow<sup>3</sup> found microscopic involvement in 25 of 48 tongue cases with palpable nodes, or 52 per cent. Phillips,<sup>4</sup> in 59 cases of buccal carcinoma with clinical metastases, found microscopic involvement in 37, or 63 per cent. Simmons,<sup>5</sup> in 22 cases of oral cancer with palpable nodes, found 12 involved, or 55 per cent. We do not grant that a man experienced in this field can decide whether enlarged nodes are involved or not, as long as there has been no break through the capsule. Therefore, we are unable to agree that without neck dissection frequent follow-up examinations offer assurance to the patient as to the time when operative intervention is indicated. All agree that once a node has become fixed the likelihood of arrest of the disease by any method is slight.

There is an interval in all these cases before metastasis occurs. Adequate local treatment will result in 100 per cent arrest at that time. Unfortunately, we have no means at present of knowing in any individual patient that metastasis has not occurred. Except in certain lip lesions, we believe that buccal cancers require some type of removal of regional nodes, on account of the danger of metastasis having occurred already.

The percentage of patients who have metastases varies with lesions in different portions of the oral cavity. It is difficult to obtain statistics on how many out of each 100 persons with these different lesions will develop metastases. It seems conservative to expect 20-25 per cent in lip cases (24 per cent found in my series); 45-50 per cent in tongue cases (47 per cent found in Morrow's<sup>3</sup> series); and 50 per cent in cheek cases (51 per cent during observation in Martin's<sup>7</sup> series). I believe that nearly all of these are doomed to death if the metastases are treated by external radiation therapy only.

The direction of metastatic spread is more definite and localized from these lesions than from most cancers in other locations. The different regional

nodes seem to act for a longer time as a bar to further spread of metastases. Technically, complete excision of the region of node involvement can be undertaken with more assurance than in most other regions. Except when involvement is found in the supraclavicular region, it is possible to excise the group of regional nodes next beyond the point where any involvement is found. This should always be our aim.

We make a practice of marking excised neck specimens so that the pathologist can tell exactly what regions are found involved. In cancer of the lower lip our custom up to a few years ago was to perform a block dissection of the neck as far down as the omohyoid-crossing of the jugular vein. This dissection was bilateral, at two operations, if the lesion involved the middle third of the lip. In 46 specimens showing metastatic involvement of the nodes, this was limited to the submaxillary or submental regions in 40 instances. In the remaining six, all showed evident clinical involvement with carcinoma in the neck before operation. Carcinoma was never found in nodes other than the submaxillary or submental when lymph nodes were not palpable in these regions before operation. Figi<sup>8</sup> states: "Extension of the malignant process through the lymph vessels draining directly into the deep cervical nodes or those entering the mental foramen rarely occurs, so that removal of the cervical nodes along with the submental and submaxillary groups is scarcely justifiable as a routine procedure." We agree with this statement.

In 1933, we<sup>1</sup> presented a group of 193 patients who had had neck dissections for carcinoma of the lower lip, with a mortality of 11.4 per cent. We find that this publication has been used as an argument against neck dissections. Later we analyzed this operative mortality further. We found that the majority of deaths occurred when some more extensive procedure than merely a neck dissection was carried out, *e.g.*, a bilateral block dissection at one operation; an extensive plastic procedure on the lip; or a partial resection of the jaw. Among 163 patients who had block dissections to the omohyoid-crossing, with no more extensive procedure on the lip at the same time than a V-excision, there were nine deaths, or 5.5 per cent. Since bilateral block dissections were effected on many patients at two operations, these 163 patients had 214 block dissections. One might, therefore, consider the mortality expected from this operation as 4.2 per cent. This included operations for all stages of lymph node involvement and was not limited to prophylactic neck dissections. If limited to the latter, the mortality would have been still lower. We might say, then, that of an expected mortality of 20 per cent from development of metastatic lymph nodes we were salvaging 15 per cent immediately after block excision to the omohyoid-crossing. We believed that this was sufficient to justify the operation, but it was still large enough to be a real argument against prophylactic neck dissection.

Therefore, as a result of our analysis of the lymph nodes found involved, we changed to a suprahyoid dissection only in those patients in whom we thought there was no evidence of metastases. This has now been effected in 81 patients with one death, or 1.24 per cent. This occurred on the fifth day

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postoperative from pneumonia, in a man, age 73. It was thought by three examiners, preoperatively, that a submental node was probably involved. No metastasis was found. The anesthetic was rectal ether.

Involved nodes were found 14 times, or 17.3 per cent. However, this operation was performed in some instances where, on account of age or general condition, it was thought that, even though nodes might be involved, a more extensive neck dissection was inadvisable. This percentage, therefore, does not represent our findings of involved nodes in prophylactic neck dissections. When involved nodes are found in the submaxillary or submental regions, we believe a further block dissection should be performed to the omohyoid-crossing as prophylaxis.

Figi's<sup>8</sup> mortality for the suprahyoid operation in 549 patients was 0.18 per cent. We believe the mortality for this operation should not be more than approximately 1 per cent. This would represent an immediate postoperative saving of 19 of the 20 per cent loss expected from cervical metastases. This low mortality effectively answers one of the arguments against prophylactic neck dissection.

What is the expected arrest when proved involved nodes are found? Since June, 1924, among the neck dissections which have been performed in carcinoma of the lower lip, metastatic involvement has been proved in 54 patients. It is fair to state that in the earlier years patients were operated upon with fixed nodes or jaw attachment, in whom an operation would now be considered contraindicated. Some of these patients were dead within a brief period, when it had been recognized at operation that the metastatic lesion, even grossly, had not been entirely removed. These factors must be taken into account in evaluating our results following neck dissection. These are shown in Table II:

TABLE II  
RESULTS IN LIP CASES WITH INVOLVED NODES

	No. of Cases
Died in hospital.....	8
Died within one year of metastases.....	6
Died within one year cause unknown.....	1
Died within two years of metastases.....	6
Died within three years of metastases.....	1
Died within four years of metastases.....	1
Died of other causes, after being free of disease over five years....	3
Followed for less than one year or lost immediately.....	9
Known to be well 12-18 months.....	2
Known to be well 18-24 months.....	2
Known to be well 2-3 years.....	1
Known to be well 3-4 years.....	1
Known to be well 4-5 years.....	2
Known to be well over 5 years.....	7
Known to be well over 10 years.....	4
Total.....	54

Out of 54 patients with carcinoma of the lower lip with proved metastatic involvement in the nodes of the neck, 14 had their disease clinically arrested

over five years, or 26 per cent. Twenty-three are known to be dead, either while still in the hospital or later of metastases, or 43 per cent. The remainder have not been followed for a five-year period, and many of these we have been unable to find. At least 26 per cent were arrested for five years, all of whom we believe would have been dead except for this treatment. Figi's<sup>8</sup> figure for five-year arrest, when lymph node involvement is found, is 39 per cent.

With operative mortality not over approximately 1 per cent for suprahyoid neck dissections, with a five-year arrest of 26-39 per cent, when nodes are found involved, we believe it is unjustifiable not to excise the regional lymph nodes, usually, in carcinoma of the lower lip. With the above considerations in mind, a routine for lower lip cases has been used in the Cancer Unit of the New York Post-Graduate Hospital for over five years.<sup>9</sup>

Metastases from carcinoma of the lip have been my assignment at our clinic. Other men have worked on metastases from other sources about the mouth. Morrow<sup>3</sup> has published his findings concerning the tongue. The metastatic spread is entirely different. With a unilateral lesion the first evident node involvement may be on the opposite side of the neck or in either supraclavicular region. I lost one patient one and one-half years after operation from a supraclavicular involvement on the opposite side. In addition to the local removal, I had performed a block dissection on the same side to the clavicle and on the opposite side to the omohyoid-crossing. Metastatic nodes had not been found in either of these neck specimens, and there was never any evidence of local recurrence. Yet, about 15 months after his original operations, a swelling developed in the opposite supraclavicular region and he declined to report for observation until it had already become fixed. We agree with Morrow that, where the condition of the patient will permit, there should be complete removal of the lymph nodes to the clavicle from both sides of the neck. The five-year survivals with this operation were 50 per cent, as compared with 30.5 per cent for bilateral operations to the omohyoid-crossing, and 14.8 per cent for unilateral operations to the omohyoid-crossing. The postoperative death rate from 1931-1935, inclusive, was 16.7 per cent. It was lowered from a previous much higher rate by undertaking more stages for completing the operative procedure. We might say, then, that, of an expected mortality of 45 per cent from metastatic lymph nodes, we were salvaging 28.3 per cent immediately after block excision of the regional nodes. Where nodes were proved involved at operation, the five-year survival rate was 11.5 per cent. Without node involvement, there were 32.4 per cent known five-year survivals.

For years I believed that cancer of the hard palate was not particularly likely to metastasize. However, in a small series MacFee and Zimany,<sup>10</sup> of our clinic, found cervical metastases in 50 per cent. Probably a block dissection to the omohyoid-crossing on the side of the lesion is what is required here as prophylaxis.

In cheek cancer our series is too small to draw definite conclusions. Prob-

ably a unilateral suprahyoid block dissection is all that is required without clinically involved nodes, except when the lesion approaches the tonsillar region. Then a dissection to the omohyoid-crossing should be undertaken. Of course, in each of these instances if involved nodes are found, further dissection is carried out to the next lymphatic block.

#### CONCLUSIONS

Radiation therapy has apparently improved but little the results in metastatic involvement of the cervical lymph nodes. Much of the surgery of this region is inadequately performed to rid the tissue of cancer cells. The plan of approach to excision of nodes needs to be varied with the location of the lesions about the mouth. The mortality from block dissections can be brought to a point where prophylactic neck dissections show a real salvage value. Five-year arrests in intra-oral cancer will show little improvement with present known methods of care until the defeatist attitude toward treatment of metastatic nodes is overcome.

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## TUMORS OF THE CAROTID BODY

CLINICAL AND PATHOLOGIC CONSIDERATIONS OF TWENTY TUMORS  
AFFECTING NINETEEN PATIENTS (ONE BILATERAL)

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THE CAROTID BODY was first mentioned by von Haller,<sup>21</sup> in 1743, and was first described in detail by Luschka,<sup>11</sup> in 1862. It is a paired organ situated at or near the bifurcation of each common carotid artery. It is supposed to attain its full development when the individual reaches the age of about 20 years, but either it does not develop in many individuals, or, if it does, it is so small that it cannot be found even at necropsy. It is normally about the size of a grain of rice and is pinkish-gray or purple. It is supplied with blood from the carotid artery and its nerve supply is derived from the glossopharyngeal nerve, the sympathetic cervical ganglion and, sometimes, from the vagus nerve.

Considerable interest has centered in tumors of the carotid body, since the original communication of Marchand,<sup>13</sup> in 1891. The literature<sup>1, 2, 5, 12, 16, 18</sup> mostly contains reports of single cases or small groups of cases, and during the last 40 years, much has been learned of the life history of these unusual neoplasms. No surgeon, apparently, has had personal experience with more than a dozen cases of the condition, and for this and other reasons it was thought advisable to review data concerning a group of 20 such tumors for which 19 patients consulted the Mayo Clinic. Twelve of the cases included in this review have been reported previously (1931) by Rankin and Wellbrock.<sup>17</sup> The series reported on by Rankin and Wellbrock included one case in which the tumor was bilateral; thus, although they reported on 12 patients, actually, their series described 13 tumors. Their case of bilateral tumor of the carotid body is included in our series; by extension, it is seen that we report on 19 patients and 20 tumors.

*General Consideration.*—*Embryologically*, the carotid body is a complex structure developed in connection with the third mesodermal arch. Early investigators believed the carotid body to be vascular in derivation. However, the observation of Stilling,<sup>19</sup> and others, that the organ contained chromaffin-positive cells has lent considerable support to the theory of origin of the carotid body in the sympathetic nervous system. At present the field is divided, but most observers concur in the belief of Kohn<sup>8, 9</sup> that the carotid body is homologous to the medullary portion of the suprarenal gland.

*Anatomically*, variations in size and position of the carotid body have been noted. Gomez<sup>6</sup> measured 26 carotid bodies and found that the average diameter was 3.5 Mm. for his series, with extremes of 8 and 0.5 Mm. In another series, Bevan and McCarthy<sup>3</sup> observed an inconstant relationship of the body to the bifurcation of the common carotid artery, but in nearly all cases the body was encapsulated and adherent to the larger arteries in the neck. In some cases the body was bilateral; in others it was unilateral. Atrophy and fibrosis were observed in the carotid bodies of elderly individuals.

*Histologically*, the chief cells observed resemble epithelial cells in being large, polygonal, and pale-staining. The cytoplasm is large in amount and is finely granular—these granules being chrome-positive in fresh tissue. Nuclei are eccentric, hyperchromatic, and frequently are vacuolated. A rich capillary network is observed and solid strands of endothelial cells are encountered. Ganglion cells, plasma cells and eosinophils have been described. All these cellular elements are grouped in the form of islands which are separated by fibrous septums springing from the capsule.

*Physiologically*, there is little or no evidence in favor of inclusion of the carotid body among the glands of internal secretion. The facts that it is frequently absent and that bilateral extirpation can be performed without the subsequent occurrence of untoward symptoms suggest that its function, whatever it may be, is negligible.

Tumors constitute the only pathologic lesion of the carotid body, and more than 200 cases of tumor have been recorded. It is not our purpose to review the literature on this subject because we believe that the material to be presented is fairly representative. We do wish, however, to enumerate, briefly, certain recent observations that have perhaps justified the inclusion of the anatomic and embryologic data previously detailed.

(1) In the presence of tumors of the carotid body the architecture of the normal body, in the matter of encapsulation and lobulation, is fairly well maintained.

(2) As in the normal body, polygonal cells and endothelial cells are present in varying numbers in the body affected by tumor—polygonal cells nearly always predominate.

(3) As in the normal body, the polygonal cells in the body affected by tumor have finely granular cytoplasm which has an affinity for chrome salts (for this reason fresh tissues always should be fixed in Zenker's fixing solution).

(4) Since these polygonal cells are probably epithelial in origin (sympathogonial derivatives), the tumors derived therefrom probably should be regarded as being chromaffinomata.

**MATERIAL.—Pathologic Aspects:** The pathologic material for this study consisted of 20 tumors of the carotid body removed surgically from 19 patients. The tumors were carefully studied grossly, and the interesting specimens were photographed. Careful measurement was made of each specimen, and notes were made on the relationship of the tumor to the carotid vessels

in instances in which resection of the latter was necessary. Multiple blocks were then obtained and placed in fresh 10 per cent solution of formalin. From these blocks, sections were cut and stained routinely with hematoxylin and eosin. In all, some 75 microscopic sections were made available for study.

No attempt is to be made herein to review the pathologic criteria that have been established for tumors of the carotid body. The observations of others were confirmed in the present series, and the important features are outlined in the following paragraphs.

Grossly, the tumors appeared as reddish-brown, lobulated, and fairly well-encapsulated nodules. The average size was 3.5 cm. in diameter, with extremes of 2 and 10 cm. In six cases, the material contained segments of the carotid vessels, and in four of these cases the vessels tunneled through, and were inseparable from tumorous tissue. In four other cases the neoplasm did not appear to be well encapsulated, and there was gross evidence of invasion of the surrounding tissue. Unfortunately, only one specimen had been preserved in Zenker's solution. This specimen was stained a light orange by the chromium salts. Nineteen tumors were unilateral; one was bilateral.

Microscopic frozen-sections stained with hematoxylin and eosin presented, with the low-power objective, two rather characteristic histologic patterns, alone or mixed. One we shall designate, for the sake of simplicity, as the "alveolar" or "insular" pattern; the other, as the "peritheliomatous" pattern. Eight of the 20 tumors had an alveolar pattern; the remaining 12 tumors had a peritheliomatous pattern.

In the alveolar, or insular, pattern, large islands of pale polyhedral cells appeared to be separated by narrow bands of connective tissue without much hyalinization. The epithelial-like islands of tumor cells occupied more than 95 per cent of the region enclosed by each field, as viewed with the low-power objective (Fig. 1*a*). Here and there the fibrous tissue was separated to permit the passage of large, thin-walled vascular sinuses which frequently were encroached upon by budding masses of tumor cells (Fig. 1*a*). A thin mantle of endothelial cells seemed always, however, to separate the tumorous buds from the actual lumens of the blood vessels. Old blood pigment was generously distributed throughout the stroma in four of the eight tumors in which this alveolar pattern was predominantly observed (Fig. 1*a*).

In the peritheliomatous pattern the cellular units, although they were somewhat alveolar, were much smaller and more irregular than they were in the insular pattern. The usual picture was that of small clumps of cells arranged in nests, or irregular strands which were separated from each other by very vascular connective tissue (Figs. 1*b* and 2*a*). In some portions these clumps of cells were seen to surround vascular sinuses. The blood vessels were everywhere abundant, but varied in size, being on an average smaller than those observed in the alveolar pattern. Hyalinization of connective tissue was a prominent feature in the peritheliomatous patterns—the tumor being

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sometimes replaced by such hyalinization to a degree seen usually only in connection with mixed tumors of the salivary glands (Fig. 2*b*). This hyaline, fibrous tissue showed a tendency (as observed by others) toward a distribution in the form of wide "bands" or "buds" (Fig. 3*a*). Hemorrhage, old and recent, was observed in eight of the 12 tumors of the peritheliomatous pattern.

Cytologically, regardless of the type, the tumors were seen to be composed mainly of polyhedral cells which had the following characteristics: (1) A

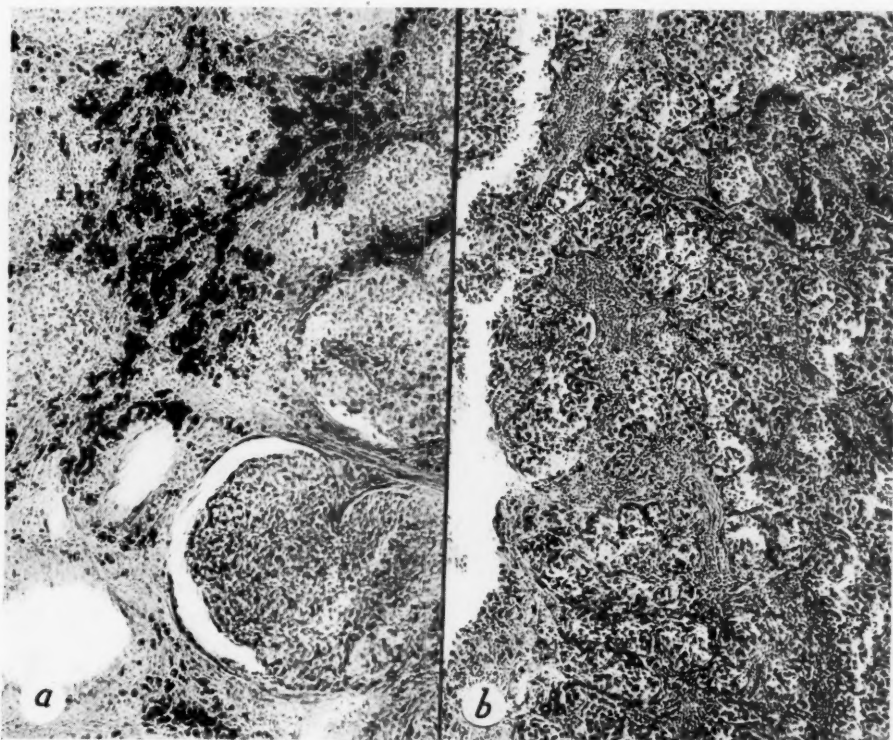


FIG. 1*a*.—Alveolar pattern in tumors of the carotid body, with large islands of tumor cells and occasional intravascular buds; a large amount of dark-staining blood pigment can be seen (frozen-section; hematoxylin and eosin;  $\times 50$ ). (*b*) Peritheliomatous pattern in tumors of the carotid body, in which small alveolar units of tumor cells separated by small capillary spaces can be seen (frozen-section; hematoxylin and eosin;  $\times 50$ ).

large amount of eosinophilic cytoplasm containing numerous vacuoles and granules so small as to be seen only with high magnification; and (2) one or more hyperchromatic nuclei.

In uninucleated forms the nucleus was generally oval in shape, eccentric in position, and had a very sharply defined nuclear membrane (Fig. 3*b*). Occasional "grooving" was observed, but did not appear to be characteristic. The chromatin appeared to be condensed in small clumps connected by delicate strands seen only on careful focusing. More than one nucleolus was the rule. In multinucleated forms, the nuclei were usually congregated eccentrically in a large cytoplasmic mass. Uninucleated and multinucleated giant cells were frequently observed, especially in the malignant tumors of the series

(Fig. 4a and b). In cases in which an excess of hyaline substance was present, the tumor cells seemed to be partially involved in the process, the cytoplasm of such cells occasionally being fused with the surrounding hyaline material (Fig. 2b), with the formation of intracytoplasmic hyaline "inclusion bodies." Aside from this type of degeneration, a second type frequently was seen in some portion of nearly every tumor studied. The nuclei in this latter type first became pyknotic and the nucleoli disappeared. At a little later stage all nuclear detail was lost and the nuclear membrane became very

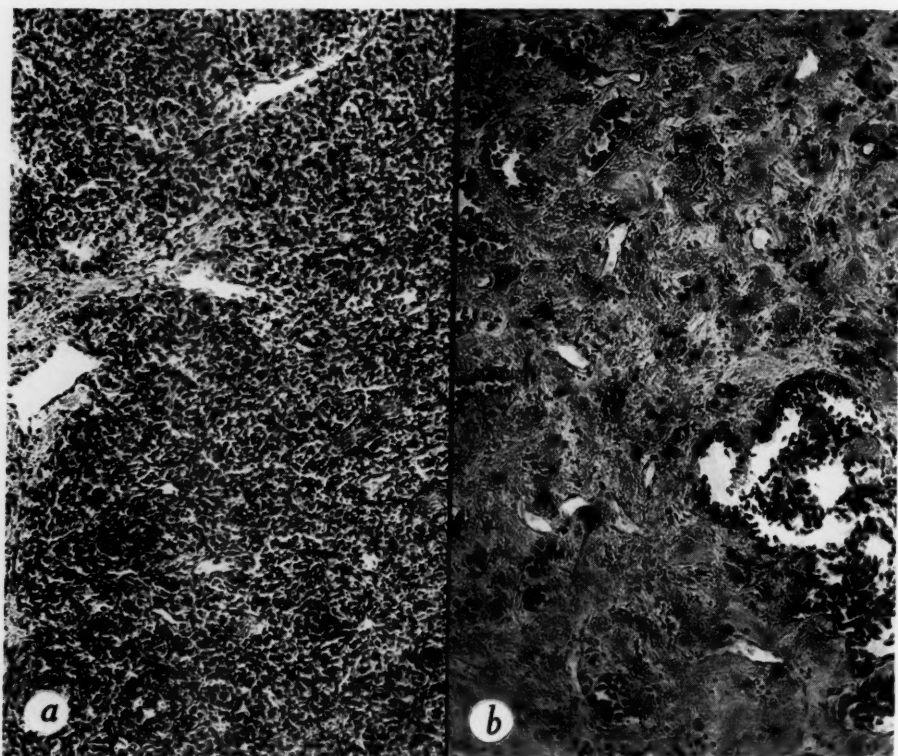


FIG. 2a.—Peritheliomatous pattern in tumors of the carotid body, in which the intimate relationship of tumor cells to the vascular spaces is more evident than in Figure 1b (frozen-section; hematoxylin and eosin;  $\times 50$ ). (b) Extensive hyaline degeneration in a tumor of the carotid body in which the "epithelial" elements appear to fuse with the masses of collagenous and hyaline fibrous tissues (frozen-section; hematoxylin and eosin;  $\times 50$ ).

shrunk and "crinkled" (Fig. 5a). At the same time the cytoplasm appeared to be swollen and somewhat basophilic, whereas the vacuoles were increased in size.

Very definite malignancy, as shown by active mitosis, cellular variation with giant cells (Fig. 4a), invasion of capsule, and the like, was present in ten of the 20 tumors in this series. However, as compared to cells of the normal carotid body, all these tumors were composed of relatively undifferentiated cells. (Perhaps it would be well, on this basis, to regard these neoplasms as being low-grade malignant lesions possessing potential powers of,



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if not actual tendencies toward, invasion and metastasis.) Two patients died of questionable cerebral metastasis. One of these patients, and an additional one, had definite local recurrence of the growth. In neither of the two cases in which the patients died, however, was permission to perform necropsy obtained, and for this reason the problem of metastasis remains unsolved.

Elements of endothelial and fibrous tissue made up the rest of the microscopic picture, with the exception of occasional nests of chronic inflammatory cells which were noted in several of the cases. As previously stated, the endothelial cells varied considerably in number and in distribution. A most inti-

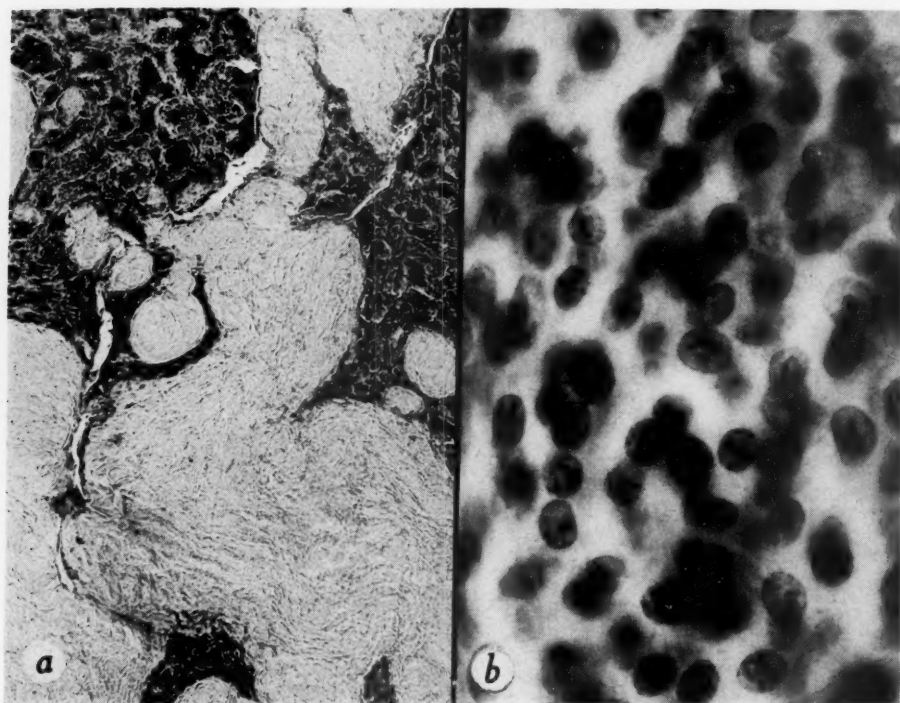


FIG. 3a.—Hyalinization in a tumor of the carotid body; the characteristic "bands" and "buds" are clearly shown (frozen-section; hematoxylin and eosin;  $\times 50$ ). (b) Malignant tumor of the carotid body in which the oval eccentric nuclei, sharp nuclear outlines, and the dense character and "speckled" distribution of the chromatin can be seen (frozen-section; hematoxylin and eosin;  $\times 900$ ).

mate approximation with tumor cells was observed in instances in which the neoplasm contained very vascular stroma. On the other hand, when fibrosis and hyalinization were extensive, endothelial elements were not so abundant. The degree of hyalinization bore no relationship to the duration of symptoms or age of the patient.

Unfortunately, 19 of the 20 tumors had been preserved in a solution of formaldehyde, a circumstance which precluded study of the chromaffinity of the granular cells. Various attempts at "rejuvenation" by means of subsequent fixation in Zenker's solution were made, but gave inconstant results. However, in the single case in which a tumor had been preserved in dichromate

solution, the size and distribution of the chrome-positive granules appeared to be exactly similar to those of the granules in the polygonal cells seen in all the remaining 19 tumors (Fig. 5*b*). It would appear, therefore, that the granules were identical in all of the 20 tumors of the carotid body.

*Incidence According to Age.*—According to reports in the literature, tumors of the carotid body occur among members of both sexes with about equal frequency. In our series, however, 12 women and only seven men had this type of tumor. Apparently, no person in any age-period is exempt. The youngest

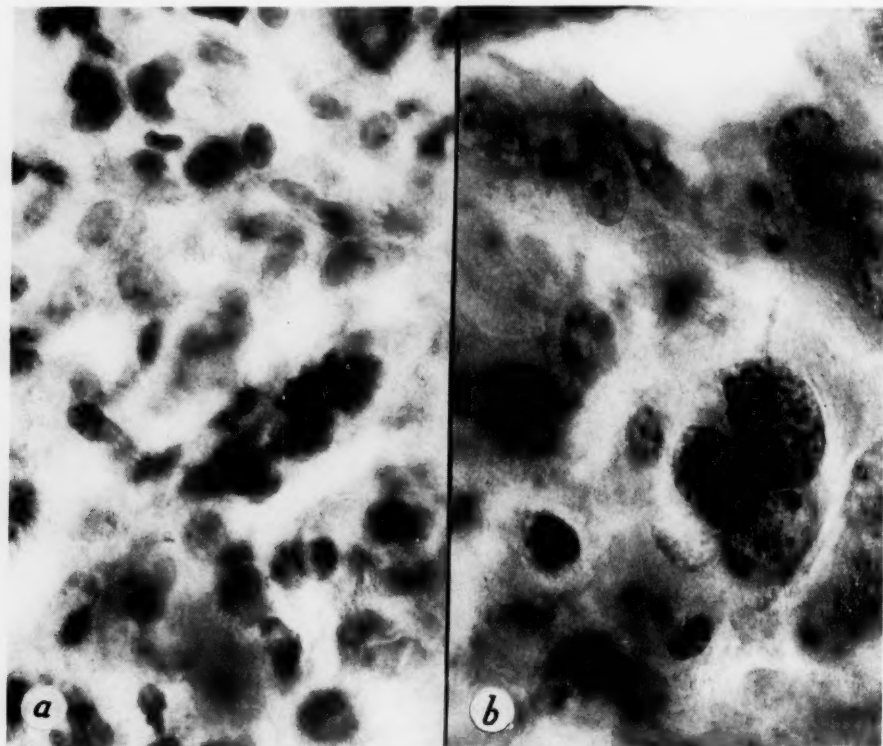


FIG. 4*a*.—Tumor of the carotid body in which multinucleated giant cells with pyknotic nuclei can be seen; in other uninucleated tumor cells in other parts of the microscopic field a similar type of degeneration is visible (frozen-section; hematoxylin and eosin;  $\times 1000$ ). (*b*) Malignant tumor of the carotid body in which hyperchromatic eccentric nuclei, multiple nucleoli, sharp nuclear membrane and granular vacuolated cytoplasm can be seen, as well as several uninucleated and one multinucleated giant cell forms (frozen-section; hematoxylin and eosin;  $\times 500$ ).

patient in the cases reported in the literature was seven years old, and the oldest was 73 years of age. The great majority of such tumors occur among adult persons, however, and according to Bevan and McCarthy,<sup>3</sup> in 70 per cent of the cases the patients are from 40 to 60 years old. In our series, the ages of the patients were as follows: Two patients were 20 to 29 years old, six patients were 30 to 39 years old, four patients were 40 to 49 years old, five patients were 50 to 59 years old, and two patients were 60 to 69 years old. The average age of the 19 patients was 45.1 years.

The tumors are usually unilateral but bilateral tumors have been reported by

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Lund,<sup>10</sup> de Tarnowski,<sup>20</sup> and Chase,<sup>4</sup> and in one of our series of cases the tumor was bilateral. The tumors occur with equal frequency on each side of the neck. In our series, which includes 19 patients, nine tumors occurred on the left, nine tumors occurred on the right, and one was bilateral. Inclusion of the bilateral tumor thus brings the total number of tumors to 20, as afflicting 19 patients.

*Symptoms.*—Tumors of the carotid body usually manifest themselves as painless, unilateral, slow-growing tumors situated in the superior, anterior

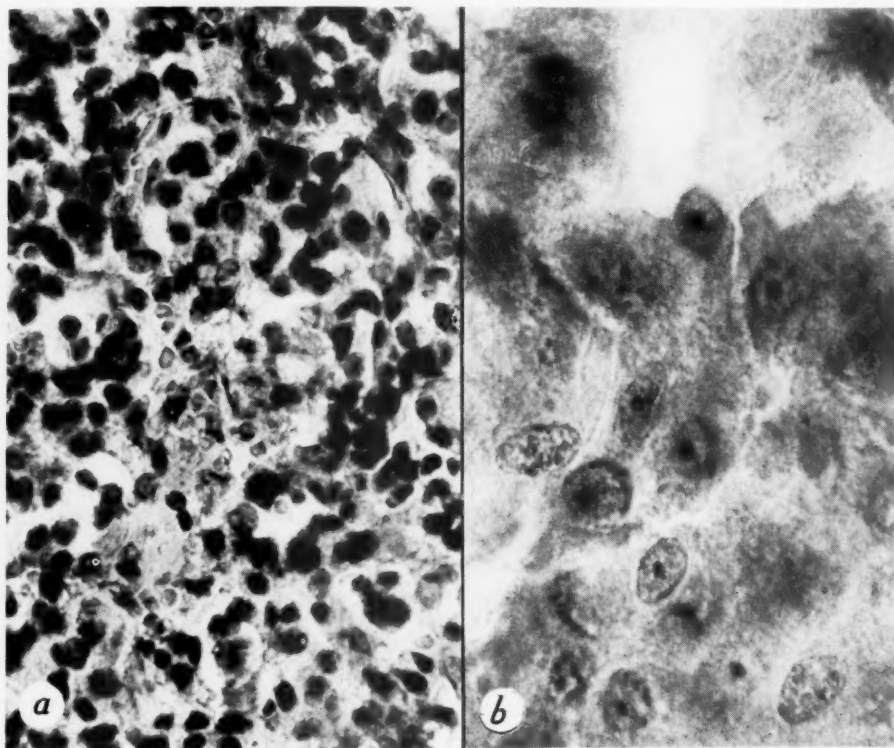


FIG. 5a.—Tumor of the carotid body in which "pyknotic" degeneration of the nuclei is shown (frozen-section; hematoxylin and eosin;  $\times 500$ ). (b) Section of tumor of the carotid body as freshly impregnated with chromate solution; the finely granular character of the cytoplasm is apparent (frozen-section; hematoxylin and eosin;  $\times 1000$ ).

cervical triangle, pushing out from under the border of the sternocleidomastoid muscle. They are ovoid or round, firm but elastic tumors and, because of their vascularity, can be compressed and temporarily reduced in size. They are deep-seated tumors and are never attached to the skin. These tumors usually have some lateral mobility, but since they are attached to the carotid vessels, they have little or no vertical mobility, and this latter characteristic has been noted by many observers as an important diagnostic point. Occasionally a bruit or thrill can be elicited, but this is not a constant observation. Often, a transmitted pulsation from the carotid arteries is evident, but it is important not to confuse this pulsation with expansile pulsation of an

aneurysm. Compression of the carotid artery below the situation of the tumor will abolish the pulsation, bruit or thrill and often will cause some diminution in the size of the tumor.

Tumors of the carotid body often are without symptoms other than gradual increase in size. They have usually been present for some time before the patient consults a physician. In our series, the tumor had been present before operation for periods of from one to 15 years; the average duration was about 5.7 years. Peterson and Meeker<sup>14</sup> have reported that in their series

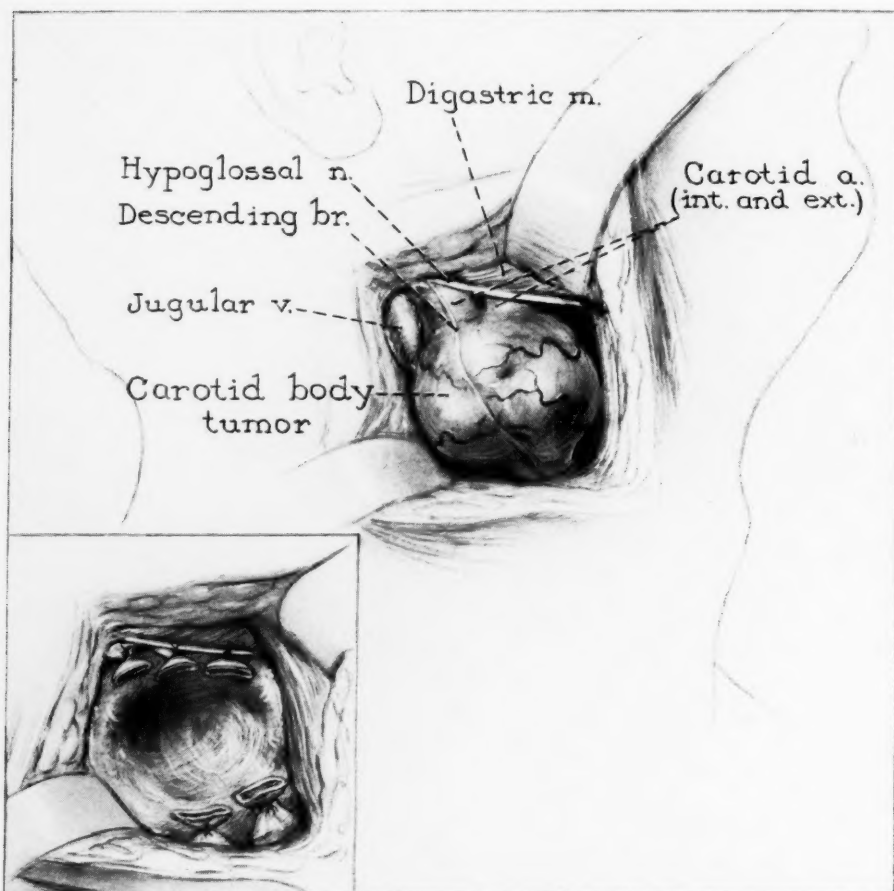


FIG. 6.—Artists' conception of exposure for removal of a tumor of the carotid body and of ligation of vessels.

the tumor had been present for about six years before operation. When tumors of the carotid body produce symptoms, such symptoms usually are caused by invasion or compression of important regional structures such as the vagus nerve, sympathetic or recurrent laryngeal nerves, or the pharynx or esophagus. Episodes of fainting, Adams-Stokes syndrome, hoarseness, dyspnea, dysphagia, cough, tinnitus aurium and headache have been reported as being symptoms referable to tumors of the carotid body and have been

attributed to compression or irritation of the vagus nerve. Horner's syndrome, exophthalmos and mydriasis have been reported, and have been attributed to disturbances in the cervical sympathetic nerves. Local, cervical or occipital pains have been held to be referable to involvement of the cervical plexus. In our series of 19 patients, only four complained of symptoms other than the increasing size of the tumor. One patient complained of a burning sensation in the throat, one of dizziness and episodes of fainting, one of paroxysmal pain in the neck and one of dysphagia and a sensation such as might be caused by an object lodged in the throat.

*Diagnosis.*—In almost every report concerning tumors of the carotid body, it has been observed that the correct diagnosis rarely has been made preoperatively. Absence of such a preoperative diagnosis probably resulted from the fact that the tumor is so rare that the possibility of its presence is not even considered by the examining surgeon. The first correct preoperative diagnosis recorded in the literature was made by Klopfenstein,<sup>7</sup> in 1895. Phelps, Case, and Snyder<sup>15</sup> found that, in the series of 159 cases they reviewed, a correct preoperative diagnosis of tumor of the carotid body had been made in 12 cases and had been considered in 14 others. In our series of 19 patients, the correct diagnosis was made preoperatively in three and existence of a lesion of the carotid body was considered as a possibility in two other instances. According to reports in the literature, the most common erroneous diagnosis has been tuberculous adenitis. In our series a diagnosis of branchial cyst was made in six cases. In two of our cases the preoperative diagnosis was aneurysm. Such a wide variety of lesions may occur in the region of the neck affected by the tumors in question that making of differential diagnosis is extremely difficult, and it is often impossible to make it until histopathologic examination of the tissue has been carried out. Diagnosis of a tumor situated in this region must include a consideration of all the various types of cervical lymphadenopathy, carotid aneurysm, metastatic carcinoma, aberrant thyroid gland, branchial cyst, branchiogenic carcinoma, neurofibroma, ganglioneuroma and tumor of the carotid body. Aspiration, or the obtaining of specimens of tumors in this region by the punch-technic has been suggested as a means of securing material for microscopic study, which would aid in the differential diagnosis of cervical tumors. We feel that the vascularity of many of these lesions and their proximity to the great vessels of the neck make such methods dangerous, and we do not recommend them. Granted that tumors of the carotid body are rare and that differential diagnosis is difficult, we believe that the possibility of tumor of the carotid body must be considered in the presence of any painless, slow-growing tumor situated in the superior, anterior cervical triangle, particularly if the characteristic signs, as previously mentioned, of lateral without vertical mobility, and decrease in size of the tumor with compression of the carotid vessels, can be demonstrated. Clinical suspicion of tumor of the carotid body necessitates careful evaluation of the surgical problem presented and permits proper preliminary treatment, so that the danger of the patient's death from cerebral anemia can be averted, or so



that paralyzes or hemiplegia, should sacrifice of the carotid vessels be necessary to extirpation of the tumor, can be avoided.

*Treatment.*—It is now generally agreed that the ideal treatment of patients who have tumor of the carotid body is complete surgical removal of the lesion when this can be accomplished without sacrifice of the carotid vessels. Absolute agreement does not exist concerning those cases in which ligation of the carotid vessels is necessary for completion of the operation. Some surgeons, notably Bevan and McCarthy,<sup>3</sup> have voiced the opinion that in those cases in which surgical exploration has shown the tumor to be inoperable without sacrifice of the carotid vessels, the incision should be closed, as would be the case after an exploratory operation, and the patient should be treated with radium and roentgenotherapy. We find little in the literature to indicate that roentgenotherapy and radium have been used in the treatment of tumors of the carotid body with much success, and Phelps, Case, and Snyder<sup>15</sup> have reported seven cases in which patients were treated by roentgenotherapy and radium without appreciable benefit. We have used both these agents in conjunction with surgical intervention very satisfactorily, but we believe that if the treatment is limited to exploration with subsequent application of radium and roentgenotherapy, cure will not result in the great majority of cases. Furthermore, it has been our experience that if the surgeon explores the lesion sufficiently to determine definitely whether or not the tumor is attached to the carotid vessels, it, usually, will be necessary to complete the removal of the tumor, even if it requires sacrifice of the carotid vessels to control the bleeding arising from these very vascular tumors. Finally, we believe that complete removal of the tumor is indicated, even if sacrifice must be made of the carotid vessels, because all such lesions in our experience have been either malignant or potentially malignant. They rarely recur or metastasize after complete removal, and the results obtained among those patients who have survived the operation are very satisfactory. In our series, there were only two cases in which local recurrence of tumors occurred, and one of the patients so affected lived for eight years, and the other for ten years, postoperatively. Peterson and Meeker<sup>14</sup> reported five cases of local recurrence in the 18 cases they reviewed. In two of our cases distant metastasis was suspected, but we have been unable to find any proved instance of distant metastasis from tumors of the carotid body.

Although we advocate complete surgical removal as the proper treatment of tumors of the carotid body, this procedure is not one to be considered lightly or to be attempted by one whose practice is only partly surgical. The proximity of these tumors to the carotid vessels, the jugular vein, vagus, recurrent laryngeal, cervical sympathetic, hypoglossal and glossopharyngeal nerves must be appreciated, and the effect of injury to these structures must be evaluated. The operative mortality in cases of tumor of the carotid body, according to Phelps, Case, and Snyder, in the 159 cases they reviewed, was 24 per cent. They found, as have all other investigators in this particular field, that practically all the operative deaths occurred in cases in which

ligation of the carotid vessels had been necessary. In our series of 20 tumors involving 19 patients, there were four deaths, a mortality rate of 20 per cent, based on the number of tumors, or 21 per cent, based on the number of patients. The cause of each death was hemiplegia following ligation of the carotid vessels. It is interesting to note, in this connection, that, in our series, sacrifice of the carotid vessels was necessary in nine instances. The average age of the patients who died following ligation was 53 years, whereas the average age of those who survived ligation was 31 years. Two patients in the younger group were afflicted by transient hemiplegia which gradually disappeared. It has been our experience that in approximately one-half of the cases of tumors of the carotid body, ligation of the carotid vessels is necessary for complete removal of the tumor (Fig. 6). Because of the risk which this procedure entails, particularly for older individuals, we believe that in any case in which tumor of the carotid body is suspected, the patient should receive proper preoperative preparation consisting of systematic compression of the common carotid artery against the transverse process of the sixth cervical vertebra several times daily for a few weeks so that an attempt may be made to develop improved collateral circulation in the brain on the affected side. Compression should be carried out for gradually increasing periods until the patient can tolerate complete compression of the vessel for long periods without experiencing faintness or loss of consciousness. We believe that application of this procedure will result in a definite decrease in the risk of surgical intervention in these cases, particularly among older individuals.

Other structures that may be injured in the course of surgical removal of tumors of the carotid body are: The internal jugular vein, the vagus nerve, the recurrent laryngeal nerve, the cervical sympathetic chain of nerves, the hypoglossal nerve and the facial nerves. As previously noted in our series, ligation of the common carotid artery was necessary in nine cases, and in two additional cases the external carotid artery alone was ligated. In six cases the internal jugular vein was ligated. The hypoglossal nerve, the vagus nerve and the recurrent laryngeal nerve were injured in one case each in our series. Phelps, Case, and Snyder reported that in the series of 159 cases they reviewed, operative injury to structures other than the carotid vessels occurred in 24 per cent of cases.

In our series of 20 tumors of the carotid body, there were ten tumors which were classified as being definitely malignant, and ten that were classified as being potentially malignant. We have found no way to determine the nature of these tumors before microscopic examination was made. The duration of the tumor before operation was essentially the same in both groups. The necessity for ligation of the carotid vessels was practically the same in both groups. The number of immediate postoperative deaths was equal in both groups. We have traced the eight patients who had definitely malignant tumors, who survived operation, and have found that two died of recurrence eight and ten years after operation. The rest were alive and

well at the time of this report. One patient has survived 15 years and another 11 years. In the other group we have been able to trace only five patients; they are alive, and have been well for from one to 14 years after operation. One patient in our series received preoperative roentgenotherapy, elsewhere, without benefit. Four of our patients received roentgenotherapy postoperatively, three received radium postoperatively and one received both roentgenotherapy and radium therapy. We cannot prove, on the basis of observations in our series, that roentgenotherapy or radium therapy has been of definite value in the treatment of the disease in question, but we believe that either type of therapy is justified if it is used in conjunction with surgical intervention.

#### CONCLUSIONS

Tumors of the carotid body are relatively rare, but the possibility of the presence of one of them should be considered in any case in which a tumor occurs in the superior, anterior cervical triangle of the neck, particularly if lateral mobility without vertical mobility of the tumor is present, if there is transmitted pulsation of the tumor, and if the tumor decreases in size on compression of the carotid vessels.

Tumors of the carotid body occur with equal frequency among members of both sexes. The majority occur among persons who are from 40 to 60 years of age. They are usually slow-growing, painless tumors, and have been present for from six to seven years before the patient consults a surgeon.

Tumors of the carotid body are always malignant or potentially malignant tumors. They rarely recur or metastasize after complete surgical removal.

The treatment of tumors of the carotid body should be complete surgical removal. The operation is delicate and dangerous because of the proximity of the tumor to vital structures in the neck. Ligation of the carotid vessels is necessary for complete removal of the tumor in about 50 per cent of cases.

Ligation of the common carotid vessels constitutes the greatest danger of the operation. We believe that in every case in which a tumor of the carotid body is suspected, the patient should have proper preliminary treatment, consisting of systematic compression of the carotid artery several times daily on the affected side for gradually increasing periods. This should be continued until the patient can tolerate complete compression for long periods without experiencing episodes of fainting or loss of consciousness. This procedure will help improve collateral circulation and will materially lessen the mortality and morbidity rate accompanying those operations in which ligation of the carotid vessels is necessary.

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## THE SUCCESSFUL REMOVAL OF A SADDLE EMBOLUS OF THE AORTA, ELEVEN DAYS AFTER ACUTE CORONARY OCCLUSION\*

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THERE IS NOW a moderately extensive literature on the clinical use of heparin.<sup>1</sup> However, instances where the use of heparin has made possible the successful removal of large emboli are not numerous,<sup>2,3,4</sup> hence, we are reporting such an occurrence.

A physician, age 32, (Hosp. No. S-41624), ran up the 20 steps at the entrance of the Hospital of the University of Pennsylvania at 8:30 on the morning of March 28, 1939. He then felt some tightness in his upper sternal region and in both upper arms. Shortly thereafter, while attending routine hospital duties he became weak and noticed more discomfort in his chest. Then he experienced severe pain under the sternum and in his arms, broke out in a cold sweat, and felt as though he could not take a full breath. He was put to bed and given 1/3 gr. of morphine sulphate.

When seen at 9 A.M. he had severe oppression in the lower sternal region and his arms felt heavy. He was pale and sweating. The pulse was 60; the blood pressure 130/90. Physical examination was otherwise normal. Nothing unusual was heard in the heart or lungs. The abdomen was soft and the extremities were normal.

At first, the diagnosis was uncertain, but the following features made it quite clear that the patient had suffered a cardiac infarction in the anterior surface of the left ventricle: (1) The electrocardiograms (Fig. 1) showed findings which are quite characteristic of such a lesion; (2) the temperature rose to a high point of 103° F. on the second day, and remained above normal for six days; (3) a definite pericardial friction rub was heard on March 29, 1939, and disappeared the next day; (4) a gallop rhythm was heard on March 31, 1939; (5) the leukocyte count on the afternoon of March 28, 1939, was 16,000 per cu. Mm., with 87 per cent of polymorphonuclear cells.

An interesting feature of the first week was the trepopnea<sup>5</sup> which he experienced. He breathed most freely and comfortably lying flat on his face with his head turned toward the left. All other positions gave him a feeling that he could not take a satisfying deep breath.

The following features were at first difficult to reconcile with the diagnosis of cardiac infarction, but in the light of the whole situation must be considered as interesting variants of the typical picture, rather than as conflicting testimony: (1) He was only age 32; (2) the pulse rate was 55 to 70 per

\* Presented by title before the American Surgical Association, White Sulphur Springs, W. Va., April 28-30, 1941.



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minute during the first day, and never rose disproportionately to his temperature; (3) the blood pressure, which was 105/80 before the attack, rose to 130/90, remained at that level for the first three days, gradually dropped to 110/70 on the fifth day, and remained there; (4) on April 1, 1939 (the fifth day), a patch of consolidation (or atelectasis) appeared at the right base, and he coughed up some rusty sputum containing a few pneumococci. The temperature chart was not obviously affected by the pulmonary lesion. Three days later the temperature reached normal.

At 6:45 A.M., on April 7, 1939, the eleventh day following the cardiac infarction, the patient awoke with a feeling of formication in the scrotum. During the next three minutes the paresthesia extended down the inside of

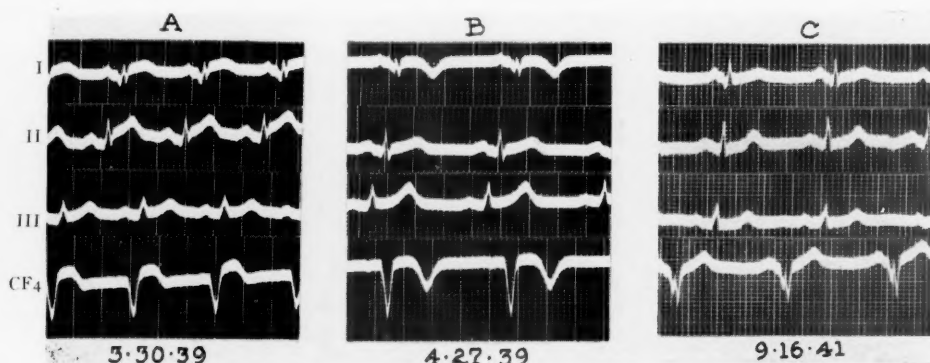


FIG. 1.—Electrocardiograms of patient described in text: (A) Tracing taken 3-30-39, two days after the onset. The RST interval elevations in leads I, II and CF<sub>4</sub> are characteristic of recent infarction in the anterior wall of the left ventricle. Lead CF<sub>4</sub> also shows a Q wave. (B) Tracing taken 4-27-39, thirty days after the onset. The RST interval deviations have disappeared. T wave inversion is present in leads I and CF<sub>4</sub>. The contour of the tracing and the changes which have taken place since 3-30-39 are confirmatory evidence of former infarction in the anterior wall of the left ventricle. (C) Tracing taken on 9-16-41 showing further changes towards normal. The T wave inversion in lead I has disappeared. The Q wave in CF<sub>4</sub> persists.

the thighs. Then it was replaced by agonizing pain in both legs. At this point the patient noticed coldness and mottling of both legs and himself made the correct clinical diagnosis. He recalled to his nurse a patient with cardiac infarction and an embolus to the bifurcation of the aorta whom they had attended together the year before, who subsequently had lost both legs and had died. After the patient had received a grain of morphine sulphate, the pain became bearable. When seen at 7:25 A.M., the penis and scrotum were anesthetic, the legs were cold, mottled, and anesthetic, and no pulses could be felt in or distal to the femoral arteries. There was no doubt that an intraventricular clot had been discharged and had blocked the aorta at its bifurcation (Fig. 2). Embolectomy was decided upon and he was taken to the operating room at 9:30.

The operation was performed by one of us (I.S.R.) under local anesthesia. A cannula was inserted into the left antecubital vein for intravenous fluid administration. Dr. J. H. Gibbon, Jr., measured the blood which was lost during the operation and controlled the rate of flow and amount of blood which the patient received. The distal end of the external iliac artery and

the proximal portion of the femoral artery of each side were exposed through a six-inch incision. In order to expedite matters, assistants were arranged for each side—Drs. J. E. Rhoads and W. D. Frazier for the right side, and Drs. N. E. Freeman and K. A. Zimmerman for the left. This greatly facilitated the operative procedures.

Two fine pieces of rubber tubing were placed beneath the vessels on each side proximal to the origin of the profunda femoris to prevent the clot, when dislodged, from passing distally, and to provide a method for hemostasis.

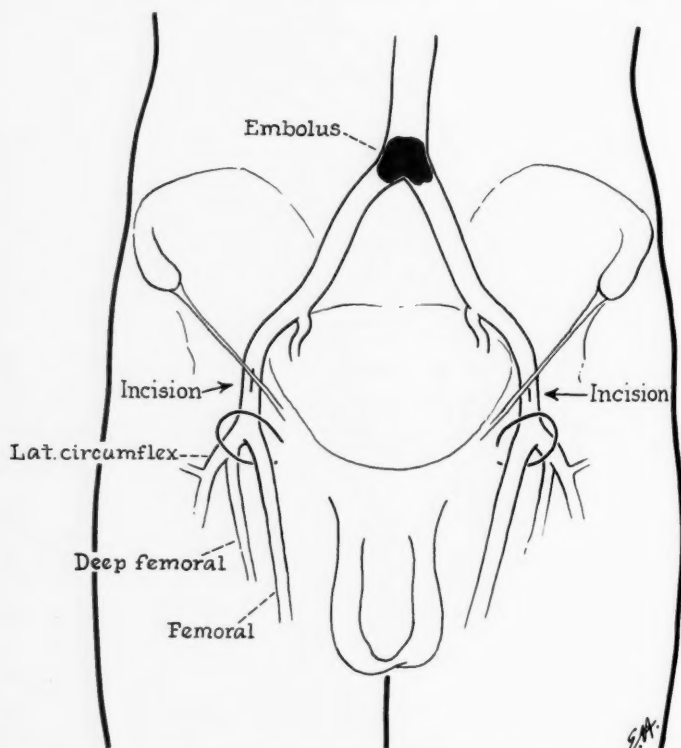


FIG. 2.—Sketch showing position of embolus and incisions for its removal.

When the artery on the right was incised in the longitudinal direction, a little bleeding occurred from the distal portion of the vessel. A modified Babcock vein-stripper (Fig. 3) was then inserted proximally until the soft substance of the thrombus was encountered. The stripper was then moved upward and downward in order to fragment the clot. When the stripper was withdrawn, free bleeding was obtained. A specially prepared catheter, the tip of which had been removed and the end carefully smoothed, was inserted toward the heart. After it had been introduced for approximately 30 cm., suction was applied and the catheter carefully withdrawn. It carried with it several masses of clot. Free bleeding was prevented by traction on the proximal rubber sling.

A similar procedure was carried out on the left side. There was prac-

tically no bleeding on this side when the artery was first incised. A catheter was introduced and a small amount of clot sucked out. A free flow of blood, however, was not established until a vein-stripper had been introduced and pushed well up several times. A considerable amount of clotted blood was drawn down and a free flow established after the artery had been sucked out once more. A final attempt to draw clotted material out of the artery was made with flexible grasping forceps but no other clot could be found. The right artery was again sucked out.

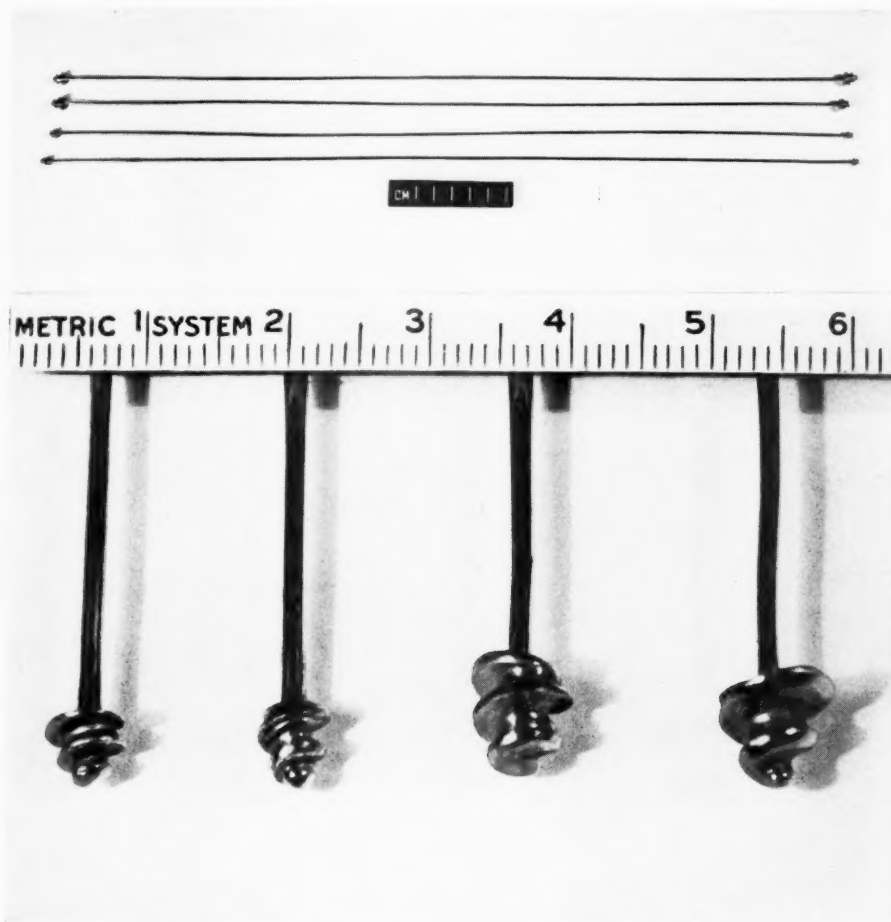


FIG. 3.—Modifications of the Balcock vein-stripper for use in fragmenting an embolus.

After a good flow of blood was obtained on both sides, the two arteries were closed with arterial silk, a double layer of continuous suture being used. Just as the suture line in the right femoral artery was nearing completion, 5,000 units of heparin (Connaught Laboratories) were introduced intravenously. Blood loss was compensated quantitatively by transfusion, the amount of blood lost being estimated by collection in a trap on the aspirator and a liberal allowance being made for blood removed on sponges.

After the last arterial suture was placed, an additional 5,000 units of heparin were given. The wounds were then closed in layers, the skin edges being approximated with interrupted black silk sutures. Despite his recent cardiac infarction, the patient stood the operation well.

Shortly following the operation, Dr. Norman E. Freeman did a left paravertebral injection with 1 per cent novocain.

Heparin was given for 11 days following the operation. Three types were used: Swiss, Swedish, and that made by the Connaught Laboratories in Toronto. It was given intravenously by the slow drip method by adding it to solutions of normal saline and 5 per cent glucose, or to 5 per cent glucose alone. The coagulation time as determined by the Lee-White method<sup>6</sup> varied during the period of therapy from 14 minutes to one hour and 13 minutes.

Although no peripheral pulses were palpable in either lower extremity immediately after operation, the color and temperature of the right leg and its motion and sensation returned to normal almost at once. On the left side, some coldness and mottling remained, especially on the dorsum of the foot. Moreover, this extremity remained very painful below the knee, and showed loss of touch sensation in this area for several days. Evidently a small embolus had escaped below the site of exposure of the artery. Suction and pressure therapy employed at intervals on this extremity under the direction of Dr. Hugh Montgomery. However, for some weeks, an area of painful erythema remained on the dorsum of the left foot.

By May 15 the patient was out of bed and was taking a few steps. He was discharged from the hospital on May 24, walking with a cane. Sensation was now practically normal in both legs. He still experienced some pain in the dorsum of the left foot, the result of a persisting ischemic neuritis.

He returned to work the latter part of September, 1939. In January, 1940, he was operated upon for acute, diffuse suppurative appendicitis. The operation was performed under spinal anesthesia, and his convalescence was uneventful.

At present, September 15, 1941, the patient has perfectly normal lower extremities. The musculature is normal. He walks without obvious disability and is working full time. He is playing golf, climbing stairs, and practicing surgery without substernal discomfort. Physical examination is entirely normal. The blood pressure is 120/80. The orthodiagram shows no cardiac enlargement. The electrocardiogram is shown in Figure 1 C.

This patient is an example of a rather remarkable recovery from a situation which at the time looked almost hopeless. He faced an appalling situation, was aware of its exact nature at all times, yet maintained the most superb morale throughout. This may have been a factor in his recovery.

*Discussion.*—It is now 24 years since McLean<sup>7</sup> in Howell's laboratory first isolated an active anticoagulant from liver. Howell, who played a minor rôle in the original work, later named this substance "heparin." In 1933, Charles and Scott<sup>8</sup> showed that this substance was present in varying amounts in a great many tissues, the ox lung, liver, and skeletal muscle, in order of the yield obtained from them. As a result of their work, a pure

preparation of heparin for intravenous use in patients became available. Heparin for human use has been made during the past few years in Canada, Sweden, and Switzerland. An active preparation is now being prepared in this country.

Heparin may be given subcutaneously or intravenously. It is inactivated by the addition of minute amounts of protamine, a point of very great importance when one wishes to bring the coagulation time back to normal rapidly.

Because of the extent and intensity of the ischemia in the lower half of the body of the patient we have just reported, it is our belief that adequate circulation would not have been reestablished without embolectomy. However, three subsequent experiences with major arterial obstruction of the lower extremities have shown us that embolectomy is not always necessary. The use of three conservative measures: (1) Heparin to prevent distal propagation of a thrombus; (2) paravertebral sympathetic block to relieve vascular spasm distal to the arterial obstruction; and (3) suction and pressure therapy to promote circulation in the affected extremity, will bring about a satisfactory result in a certain proportion of these patients.

The decision as to whether to persist with conservative therapy, or to resort to operation, depends upon whether or not there is evidence of continuing improvement in the circulation. If this fails to occur, operation should be carried out, for after a period of three to five hours, changes in the intima at the site of the occlusion may result in further thrombosis, despite the use of heparin following closure of the vessel.

The success which was achieved in this patient was possible only because of the excellent aid given by many individuals, only a few of whom are mentioned in this report. We are indebted to Drs. Doane, Behrend, Sappington and Whipple, who furnished the initial supplies of heparin.

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## REFLECTIONS ON GASTRODUODENAL SURGERY\*

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HONOLULU, T. H.

SIXTY YEARS ago the first stomach operation was performed. During the past half century an immense amount of work has been done and a voluminous literature has accumulated on this important subject. It seems fitting that, at this Congress, the sixtieth anniversary of the first stomach operation should be commemorated in a modest way, by presenting a bird's-eye view of what has happened to the human stomach since 1879.

Some of us here to-day were youngsters on April 5, 1879, when the courageous French surgeon, Jules Péan, performed the first gastric resection for cancer of the pylorus. His patient lived four days and died of exhaustion. It was not until three years later that Billroth, in 1881, performed the same operation and acquired the distinction of doing the first "successful" operation of the kind—which has been known ever since as the Billroth No. I. But, his patient died in less than four months of carcinomatous peritonitis. It would seem in all fairness, as the immediate success of Billroth's operation was terminated by the death of the patient in a comparatively short time, that Péan ought to have some recognition and that the operation might properly be designated as the Péan-Billroth procedure. In the same year, 1881, young Antone Wölfler, 31 years old, thrilled at the idea of emulating his chief, the giant Billroth, attempted the same operation. He found the tumor fixed and the liver involved and was regretfully beginning to close the abdomen when Nicolodani, one of the assistants, whispered something in his ear. Wölfler picked up the jejunum, brought it across the front of the colon with a long loop and attached it to the anterior surface of the stomach, thus giving birth to gastro-enterostomy, an operation which has caused much joy and much suffering. Heineke, in 1886, and Mikulicz, a year later, working independently, devised pyloroplasty, and so in a space of a few years, all the standard stomach operations were born.

The idea of side-tracking the malignant obstruction, first formulated by Nicolodani and carried out by Wölfler on that fateful day, September 27, 1881, was applied by Rydygier, in 1884, for a benign obstruction. Doyen, of Paris, in 1893, employed the operation for gastric ulcer without obstruction. This started a lot of trouble and the story of gastro-enterostomy is one of the most amazing chapters in the history of surgery.

In the early part of the century, the furor of gastro-enterostomy spread over the surgical world. People with stomach ailments, real or imaginary, felt more or less in disgrace until they had had this operation performed.

\* Read before the Third Congress of the Pan-Pacific Surgical Association, Honolulu, T. H. September 21, 1939.

House surgeons felt that they had not gained the goal of their ambition until they had undertaken their first gastro-enterostomy. It was a favorite subject of conversation at dinner parties. Not only was the operation employed where it was not needed, but it was often very badly performed. It is recorded that, needlessly, this anastomosis was performed in the following conditions: Functional disorders of the stomach, when the symptoms were due to other conditions such as appendicitis, gallstones, and tuberculosis of the intestines. Cirrhosis of the liver with hemorrhage, splenic anemia, tabes dorsalis, lead poisoning, prolapse of the kidney, colonic adhesions, epigastric hernia, and even vomiting of pregnancy.

It was bad enough to employ the operation where it was not wanted, but to perform it badly was adding insult to injury. It is recorded that the loop was made too short; the loop was made too long; or that the loop was twisted. The stomata were badly placed, too near the pylorus and not at the most dependent part of the stomach. The stomach was attached to various parts of the small intestine and even to the colon. Some of the results were terrific. Hemorrhages, primary and secondary, vicious circle vomiting due to technical errors, internal hernia, and fixation by adhesions of the loop, were some of the disastrous sequelae and, in 1899, Braun first described "marginal ulcer." More than any other surgeons, Moynihan in England and W. J. Mayo in our country taught the profession how to perform the operation properly, and the adoption of Mayo's method of running the efferent loop downward and to the left reduced the number of twists and kinks.

Strangely enough, when gastro-enterostomy was born, a rather new disease appeared on the surgical horizon in the light of duodenal ulcers. Rokitansky, the great pathologist of Vienna of the last century, who, according to Gerster, is credited with having performed 30,000 autopsies, mentioned only hemorrhagic erosions of the duodenum, and Virchow wrote nothing at all on the subject. Ziemssen, in 1876, stated that "ulcer of the duodenum is a comparatively rare disease, the proportion to gastric ulcer being hardly one to thirty." William Pepper of Philadelphia, in 1889, stated that not more than 70 authentic cases of duodenal ulcers had been reported. In our student days, the standard text-books mentioned duodenal ulcers only in their relationship to burns. Osler's Textbook of Medicine, 1899 edition, described duodenal ulcers with gastric ulcers and stated that "the duodenal ulcer is less common than the gastric ulcers." He also stated that it is more common in women than in men in the proportion of six to four. Little or no instruction on duodenal ulcers was given in the medical schools at the beginning of the century. Although some of the ulcers may have been missed, it does not seem possible that they were as prevalent half a century ago as they are now. The old fellows were keen observers and certainly would have found them had they been there. We now believe that the incidence of gastroduodenal ulcers predominates in the male sex in the proportion of four to one, that duodenal ulcers are ten times more common than gastric ulcers, and autopsy

reports state that ulcers or scars of ulcers are found in from 2 to 20 per cent of all postmortem examinations.

The history of the technic of stomach operations is an interesting one. Moynihan records that, 50 years ago, he witnessed a pylorectomy for cancer in which 200 silk sutures were used to unite the duodenum and the stomach. In 1892, Murphy invented his famous button, which adorned every instrument table in the surgical world. I well remember 40 years ago, in the old New York Hospital, attending a clinic of Professor Robert F. Weir, in which he gave a laudatory lecture on the Murphy button concluding with the introduction: "And now, gentlemen, I have the pleasure of presenting to you the inventor of this button." With that, a tall, distinguished looking man with a gray, closely cropped beard parted in the middle, arose from his seat in the amphitheater, bowed, and manifested his appreciation of the tumultuous applause of the demonstrative medical students of our day. The Murphy button taught surgeons facility in handling conditions in the abdomen. According to Moynihan "it gave a convincing demonstration of the essential simplicity of the process of visceral union. By using the button we learned how safely and how rapidly the peritoneal junction took place; there was no need, as it was now perfectly evident, for the hundreds of stitches that all surgeons were using. Firm, even approximation for a very few days would lead, the button showed beyond a doubt, to a permanent and secure fusion of the opposed viscera. It is not the least exaggeration to say that Murphy revolutionized the methods of visceral anastomosis, and was partly responsible for giving that impulse to abdominal surgery, which in later years has carried it so far." After surgeons had learned the above quoted facts, the use of mechanical appliances had played their part. Moynihan further says: "To Murphy, above all other surgeons, for his instrument is one of the most ingenious mechanical contrivances ever invented, we should gratefully acknowledge the debt we owe. Without the knowledge of his button, the surgery of the stomach and the intestines would never have reached its present stage." Poor Murphy, one of the most brilliant men of his time, a tremendously hard worker, died at the age of 59 of overwork, and his button, which at one time was used all over the world, is not even mentioned in modern text-books.

Our experiences in gastroduodenal surgery here in Hawaii may be likened to a cross-section of stomach surgery since the days of Péan. The first gastro-enterostomy was performed in 1905. The first partial gastrectomy, Billroth No. II, was performed in 1908. In the same year, a gastro-enterostomy was accomplished without clamps. In the "horse and buggy days," encountering an enormously dilated stomach with a contracted pylorus in a poorly equipped hospital, without any stomach clamps available, a posterior gastro-enterostomy was performed, and the patient made a very smooth recovery and went back to her position as a lei seller. I believe that she still functions in that capacity and may have helped to decorate some of you gentlemen on your arrival. At that time, there were many clamps, the Roosevelt, Little-

field, Scudder, Doyen, Hartman, Mayo-Robson, *etc.*, and it was heresy not to use them. As I felt that I had committed a heresy, I kept quiet about it. At the same time, I was impressed by the ease with which the operation could be accomplished, and with the smooth convalescence of the patient. Since then I have rarely used clamps. In 1917, Rutherford Morrison, the brilliant English Surgeon, wrote as follows: "The greatest authorities advocate the use of clamps, and they offer many advantages. There is, however, a danger of internal hemorrhage after the operation has been completed, and although this may be a negligible risk in the hands of experts, it has so often occurred to my knowledge that, notwithstanding the most powerful advocacy to the contrary, I feel safer in doing the operation without clamps and tying each spouting vessel separately before completing the operation." If clamps are unnecessary, why use them? It always makes me shudder to see a nice, velvety piece of jejunum held like a vice in vicious looking instrument. I wonder what happens to the delicate tissues involved, if some of the tiny blood vessels are not crushed and the sympathetic nerves bruised and insulted. It is recorded that some marginal ulcers have appeared within two weeks of the operation. It is thus possible that this condition was aroused by the damage done by the clamps. Some gastro-enterostomies do not do well after operations. Balfour, in his monumental book, writes as follows: "In some cases, obstruction apparently may be complete and may persist even with discontinuing of food, lavage, or intravenous administration until for some unexplained reason the gastro-enteric stoma begins gradually to function and finally the difficulty is entirely corrected." May not this condition as above described be due to the physiologic resentment of the stomach and intestine against having been squeezed so tightly and so long?

In this most fascinating chapter of abdominal surgery, we have sat here on the sidelines and watched the contest going on, dashing into the fray now and then. In wondering what it is all about, we have tried to follow the voluminous literature on the subject and have concluded that there is hardly any disease which has so many causes as peptic ulcer. The different assigned causes may be divided into the category of predisposing and exciting. In the first group fall the so-called constitutional predisposition, the ulcer diathesis, the hypertonic stomach with active peristalsis, rapid emptying, hyperchlorhydria, hypersecretion, and along with this condition a relatively deficient blood supply of the ulcer area. The vessels supplying the lesser curvature are long and slender, and are mostly end-arteries going through the muscular layers to the mucosa. According to Alvarez, the mucous membrane of the lesser curvature is fastened to the muscle much as the skin of the palm of the hand is fastened to the fascia. Then there is adrenal overactivity, vagatonia, and the vasoneurotic diathesis.

In the group of exciting causes, there occur trauma, external and internal, from food too hot, too cold, and too rough, focal infections, including diseased gallbladders and appendices, bacterial infections, preceding chronic gastritis and duodenitis, derangement of the nervous system, worry, fatigue, emotional

disturbances, organic brain disease such as tumors, alcohol and tobacco and, of course, vitamin deficiencies and endocrine disturbances.

Some writers have gone so far as to describe the physiognomy of the ulcer subject "with high malar prominences, a thin often wheezened face, an anxious look, poor nutrition, and an energetic demeanor." About 100 years ago, Dupuytren noted that duodenal ulcers sometimes developed after severe burns. Then this condition was described by Curling, in 1842. This is the one cause that all authorities agree on without controversy, and no one has satisfactorily explained the mechanism of it.

Like the coronary arteries, the ulcer producing portion of the stomach and the duodenum is subject to the great strain of wear and tear. The Germans called this area the "*magenstrasse*," and this part of the stomach may be thought of as a curving highway with a more or less continuous stream of automobiles passing over it. These automobiles vary in weight and speed. Erosions appear in the road surface and increase in size as they are subjected to added wear and tear. The pavement gives out and ulcers appear like chuck-holes of the roadway. The causes of the ulcer are as numerous as the different makes of automobiles passing over the highway.

With all the knowledge that has accumulated during the last 50 years, we have settled down to some definite conclusions and indications. History repeats itself. Over 70 years ago, Cruveilhier, whose name is still given in France to peptic ulcers, laid down the principle that peptic ulcers are curable; that dietary regimen is of paramount importance in the treatment and prevention of recurrence. He was also the first to recommend a milk diet. What can we conclude from the enormous mass of material and experience that has accumulated in the last 50 years?

(1) When Walter B. Cannon, in 1897, first gave a goose some bismuth to swallow so that he could study the process of deglutition, he started something which has been most valuable to the human race, and the roentgenologic diagnosis of stomach lesions is now over 90 per cent correct. Cancer of the stomach can be recognized early enough to be operated upon successfully.

(2) Ulcers can be cured by medical treatment in 50 to 80 per cent of the cases if the patient cooperates. Of patients treated in the earlier stages 85 to 90 per cent are curable. Essentials for a cure are lightening of physical and mental strain, a careful diet, and avoidance of alcohol and tobacco.

(3) What group of patients should especially not be operated upon? Young patients with small stomachs, small ulcers and hyper- or even normal acidity should not be subjected to gastro-enterostomy on account of the danger of jejunal ulcers. One of our patients had a profuse hemorrhage from a marginal ulcer following a gastro-enterostomy performed on the mainland 18 years previously, but this record has been superseded by Finsterer, who records a gastric hemorrhage 28 years after the primary operation.

(4) What patients should be operated upon? Those who have the following complications:



- (a) Acute perforations of gastric and duodenal ulcers and the sooner the better.

Should gastro-enterostomy be performed at the same time? No, unless, in exceptional cases, when the repair of the perforation produces a definite pyloric obstruction.

- (b) Persistently recurring hemorrhage in spite of good medical treatment.

In this connection, it is interesting to call attention to the radical revision of treatment of gastric hemorrhages by Meulengracht, who reduced the mortality of hemorrhagic duodenal ulcer to 1 per cent. In a series of 251 cases, the mortality with orthodox treatment in the same city for a similar four-year period was 7.9 per cent. Instead of starvation of the stomach plus transfusion, he feeds his patients meat balls, puréed vegetables, omelets, *etc.*, and allows them to eat as much as they want. In a few cases in which we have employed this treatment, we have been impressed by the results and believe that it is worth trying, as the mortality from hemorrhage runs anywhere up to 16 per cent, according to different observers.

- (c) Where pain persists in spite of good medical treatment, and the patient is becoming weakened from under-nourishment and suffering.
- (d) Where there is organic pyloric obstruction not relieved by medical measures.
- (e) In gastric ulcers where the possibility of malignancy can not be eliminated. This especially pertains to ulcers of the greater curvature.

(5) What operations should be performed on the stomach when these conditions exist, and it is required that they be remedied? The stomach is a highly developed and sensitive organ and is very resentful of any liberties taken with it. Each case should be studied on its own merits, and unless the proper surgical procedure is applied to it, there is bound to be trouble.

Gastro-enterostomy.—An operation that carries with it the hazard of marginal ulcers supervening anywhere from 12 days to 28 years after its performance, should be looked at askance. The percentage of patients developing these ulcers varies in different reports from 3 to 40 per cent. Alton Ochsner thinks that 3 per cent is too low a figure and that an additional 25 to 30 per cent who have not been relieved by the operation, are sufferers from marginal ulcers.

(1) In ulcers of the lesser curvature, simple excision is condemned as producing a "lop-sided" peristalsis with impaired emptying and a gastro-enterostomy, in addition, is recommended. Fortunately, gastro-enterostomy in this group of cases is rarely followed by jejunal ulcer.

(2) In older people with marked pyloric obstruction, dilated stomachs,

and hypo- or anacidity, gastro-enterostomy is a satisfactory procedure. As time goes on and duodenal ulcers are recognized and treated earlier, perhaps there will be fewer patients in this group.

(3) In some cases of cancer of the stomach where a two-stage operation is advisable, gastro-enterostomy is indicated for the first stage.

With these three exceptions, we would say, "Don't do a gastro-enterostomy!"

For less severe cases, a plastic operation on the pylorus of the Horsley or Finney type, combined with excision of the ulcer, is far less apt to be followed by disagreeable consequences.

For severe cases with old, hard duodenal ulcers, fixed to the pancreas, subtotal gastrectomy is indicated with the removal of three-fourths to four-fifths of the stomach. In exceptional cases, the Billroth No. I and No. II and Devine's antral exclusion may be called for.

Time allows only a few minutes in which to mention our favored method of gastrectomy. Of the fourteen or more methods, we employ what is known as Moynihan No. II, as described in his admirable book on Abdominal Operations. The loop of the jejunum is carried in front of the transverse colon and attached to the cut end of the resected stomach, the loop running from left to right and not from right to left as in the original Pólya. The proximal end of the jejunal incision is attached at the greater curvature and the distal part of the jejunal attachment is made at the lesser curvature. The cut end of the stomach may be partly closed or the jejunal attachment may be made along the full length of the resected area. This, I believe, is the method favored by Dr. Frank Lahey, although he calls it the Hofmeister operation. It is easy of execution, not complicated, does not involve opening the transverse mesocolon, and is usually followed by prompt reestablishment of gastric drainage with less disturbance and troublesome symptoms than follow more complicated methods.

# LYMPHOGRANULOMA VENEREUM: TREATMENT OF SEVERE CASES OF ANORECTAL TYPE BY A MUCOSAL-STRIPPING OPERATION\*

A PRELIMINARY REPORT

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It is only recently that lymphogranuloma venereum has become generally recognized as presenting a serious problem in public health, especially among the colored race. Statistical reports on groups of cases by the hundred are appearing almost every month in the literature.<sup>3, 16, 17</sup> Figures emphasizing the frequency of the disease are given by Gray,<sup>1</sup> who found that out of 790 patients submitted to the Frei test in a city hospital in St. Louis there were positive reactions in 40 per cent of the colored patients, and 3.4 per cent in the white patients. Gray further found, as have others,<sup>2</sup> that a very large percentage of people who contract the disease entirely recover from it, and all that remains as evidence is the positive Frei test. Of those who do not symptomatically recover, and who go to the clinics for treatment, most of them will have the disease in a chronic form—their symptoms not being severe enough to require hospitalization. But not all the chronic cases will be so fortunate—a number of them will reach our hospital beds in a miserable condition. The patients are usually colored and they are destitute; therefore, one finds most of them in the charity hospitals. However, even at the Vanderbilt Clinic and Presbyterian Hospital in New York City, Dr. Helen Curth and Doctor Gutman<sup>3</sup> observed more than 200 cases of lymphogranuloma venereum during the period 1931–1938. They state: “The largest number of more than 100 were tertiary cases showing rectal strictures, chronic ulcerations of the genitals, elephantiasic swelling, proctitis, arthritis and systemic manifestations.”

Of the tertiary, or severe cases, we are at this time interested in those of the anorectal type. These usually have a rectal stricture, though some cases do not. The rectal stricture may vary in degree and extent, but in many cases intestinal obstruction of some degree exists. There are one or more abscesses, fistulae or sinuses about the ischio-rectal region. There are multiple condylomata about the sinuses and fistulae, and these condylomata are frequently at the anus and inside the rectum. Two of our cases had 18 and 20 fistulae, respectively, about the anus. Moreover, these patients are suffering from extreme loss of weight, a low grade fever, secondary anemia, secondary infection and frequently from other diseases, such as syphilis, carcinoma, or cardiovascular-renal disease.<sup>3</sup> They have pain from the local inflammatory process and pain in the abdomen from obstruction. In fact, what usually brings these

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\* Read before the New York Surgical Society, October 9, 1940.

patients to the hospital is the distressing local symptoms and the symptoms of intestinal obstruction. In a certain number the bowel perforates and the patient dies. Warthen<sup>4</sup> states that practically every large series of cases has included fatalities from peritonitis. Gutman<sup>3</sup> noted three such cases from the Presbyterian Hospital in New York, and, also, remarks that death following peritonitis is not rare. In some cases the disease progresses up the colon. Cases are reported with liver abscesses, renal involvement and systemic manifestations of various kinds.<sup>3</sup>

Once a case has become as severe as described, we find that he shifts from one hospital and clinic to another. This is because a satisfactory method of treatment is not available. Of our group of these severe cases, we find the history extending back over a period averaging four years.

Unfortunately for the patient the simple procedures do not always turn out so innocuously. Dilating their rectal strictures frequently only causes more scar tissue to form and eventually the state is reached where dilatation amounts to tearing and not stretching. With a colostomy of the ordinary loop-type, there is no reason why the disease cannot extend along the mucous membrane past the colostomy. After incision and drainage of the abscesses and fistulae, they are notoriously slow in healing, and, in fact, may not be expected to heal because of stricture, condylomata, and the disease existing inside the rectum. Frequently the proctitis apparently clears up, but often fibrous strictures of the rectum follow, and series of from 86 to 215 cases at a time have been reported.<sup>5</sup> It is now thought that a great many so-called gonorrheal and luetic strictures of the rectum of the past were in reality due to the virus of this disease.

Some progress is being made in the conservative treatment. Cases successfully treated by diathermy and sulfanilamide have recently been reported.<sup>6, 7, 8</sup> But it is one opinion that a certain percentage of these cases are going to require major surgical measures despite any medical treatment yet discovered.

The first surgical attempt to treat the disease was made by performing a simple loop-sigmoidostomy. The fecal current was thus shunted and the patient improved. Theoretically then, the symptoms might subside, and a re-establishment of the continuity of the bowel could be effected. However, we have operated on this assumption several times and have always been disappointed because the minute the fecal current passed down again through the old diseased rectum the local symptoms of infection and obstruction returned.

In chronic fibrous stricture without abscesses and fistulae, a local excision by the Whitehead type of operation has produced good results.<sup>5</sup> Also, in this type of case, a plastic operation on the rectum by a posterior approach has given good results in a small number of such cases.<sup>10</sup>

Warthen reports ten cases of rectal stricture treated by obliteration of the cul-de-sac or rectovesical pouch and colostomy.<sup>4</sup>

At first, bold excision, of the abdominoperineal type, resulted in such a high

operative mortality that this operation was quickly abandoned. More recently, however, several cases successfully treated by this method have been reported.<sup>11</sup>

Barber and Murphy<sup>12</sup> have reported 35 one-stage sacroperineal resections and 31 abdominal colostomies followed by sacroperineal resections. Their hospital mortality was 14.3 per cent.

Edwards and Kindell<sup>13</sup> have reported six cases operated upon by the Lockhart-Mummery<sup>9</sup> procedure. In all a loop-colostomy was first performed. One of their cases failed to survive the operation.

Our experience with these severe rectal cases has convinced us that the following points are true: The operative procedure must be undertaken in at least two stages; a colostomy has to be performed as a first step; an end-colostomy is better than the loop-type because the disease cannot travel upwards from the lower segment and fecal soiling of the lower segment is absolutely avoided. This colostomy will not cure the patient as the local process continues. The patient, however, will greatly improve and gain weight. The secretion of mucus from the distal segment is most annoying to the patient and adds to the number of daily dressings; also, the mucous membrane is a good medium for the virus of the disease. Any operation that opens into the peritoneal cavity during the excision of the lower segment is dangerous, and should be avoided because of the marked infection in the local lesions. The deep lymphatics and those of the mesentery and inguinal region are usually involved, therefore, even a block excision, as that of the abdominoperineal type, cannot remove all the disease. If the rectal dilatation has been carried out over a period of years, then the mucous membrane at the site of the stricture may be greatly damaged, otherwise the mucous membrane covering the rectal stricture may be intact. However, the mucous membrane below the stricture is commonly the seat of ulceration, condylomata, and multiple fistulae.<sup>14</sup> It is possible, therefore, in some cases to remove the mucous membrane covering the stricture. Lastly, it is our experience, and the experience of others,<sup>12</sup> that after removal of the rectum and laying all abscesses and fistulae open to the air, they will completely heal. On these principles we have developed the following technic:

An end-colostomy is first established. This is essentially the same operation as the first-stage of Lahey's procedure for removal of carcinoma of the rectum.<sup>15</sup> At this time we excise all of the sigmoid between the proximal and distal stomata. We do this because we find the colostomy functions better with a short pouch left inside the abdomen—the bowel empties better and there is less tendency to prolapse afterward. This type of colostomy separates the normal and diseased ends of the bowel a sufficient distance to prevent any contamination (Figs. 1 and 2). At this time any acute abscesses about the anal region are incised and drained because, in doing so, absorption is decreased and the patient is made more comfortable. The distal segment is irrigated twice a day with 2 per cent aqueous solution of mercurochrome (Fig. 2). This is the best of all the simple chemical solutions that we have employed.



Great improvement usually follows the first stage, so that, within a few weeks, the second stage of the operation may be performed. This stage may be described as a mucosal-stripping operation (Fig. 3). An incision is made about the lower colostomy opening. The mucosa is identified and then stripped away from the muscularis and peritoneal layers by blunt dissection. This is accomplished with surprising ease. We have stripped, on two cases, 23 inches of mucosa without damaging the other layers and without enlarging the suprapubic incision (Fig. 11). There are two reasons why this stripping can be so easily accomplished: First, the bowel behind one of these rectal strictures is

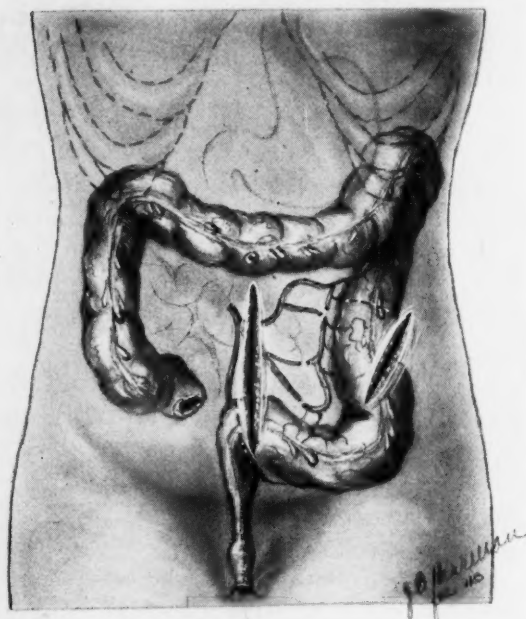


FIG. 1.—First stage of operation. Exploration of the abdomen through midline incision. Removal of most of the sigmoid, as shown by dotted lines. Proximal stump of sigmoid brought out through left McBurney incision, and distal stump brought out through lower angle of midline incision.

greatly hypertrophied, due to the years of back pressure and the effort of the bowel to force the intestinal contents past the stricture. This hypertrophied condition identifies the layers more definitely. Second, the blood vessels and nerves run along the muscularis and at intervals dip through the muscle layer and the loose submucosal tissue into the mucosal wall (Fig. 10). These small, penetrating vessel branches do not bleed a great deal when divided. If a branch requires it, it may be ligated. After all the mucosa possible has been stripped from above, a small catheter or bougie is introduced in the tube of stripped mucosa and pushed

down through the rectum out the anus (Fig. 4). The mucosa is then tied or sutured to the proximal end of the catheter. The patient is then placed in the lithotomy position. All surrounding condylomata and fistulous openings are, for the moment, not disturbed. An incision is made about the anus at the mucocutaneous junction, very much like the beginning of the Whitehead procedure (Fig. 5). As soon as the mucosa is well-identified and freed, anterior and posterior incisions are made in the midline and the sphincter muscles divided and retracted laterally. The dissection is then carried to the levator muscles and, if necessary, these may be divided anteriorly and posteriorly. Meanwhile the rectal mucous membrane is further stripped by pushing the muscularis back from it (Fig. 6). At this stage the anal end of the catheter is pulled downward, bringing with it the upper end of the mucosa—

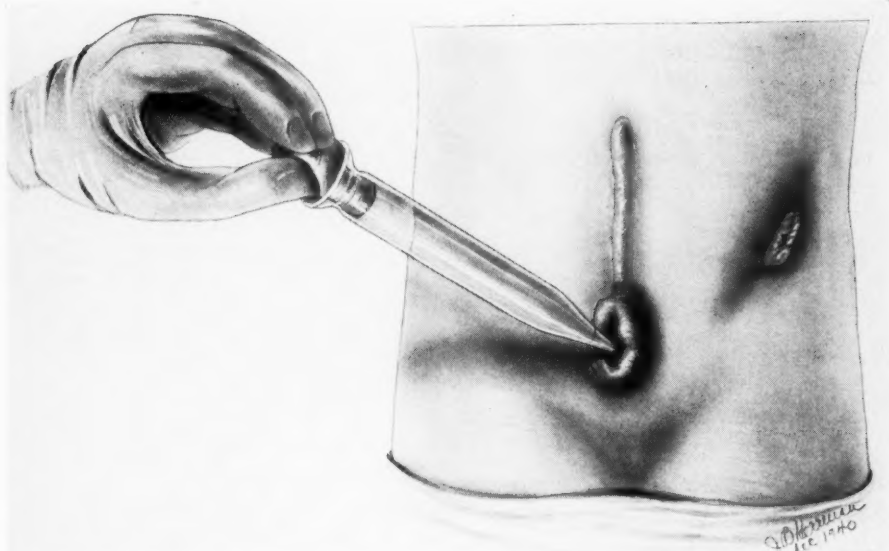


FIG. 2.—Left McBurney, permanent, short pouch, colostomy. Lower segment is irrigated twice daily, usually with aqueous solution of 2 per cent mercurochrome.

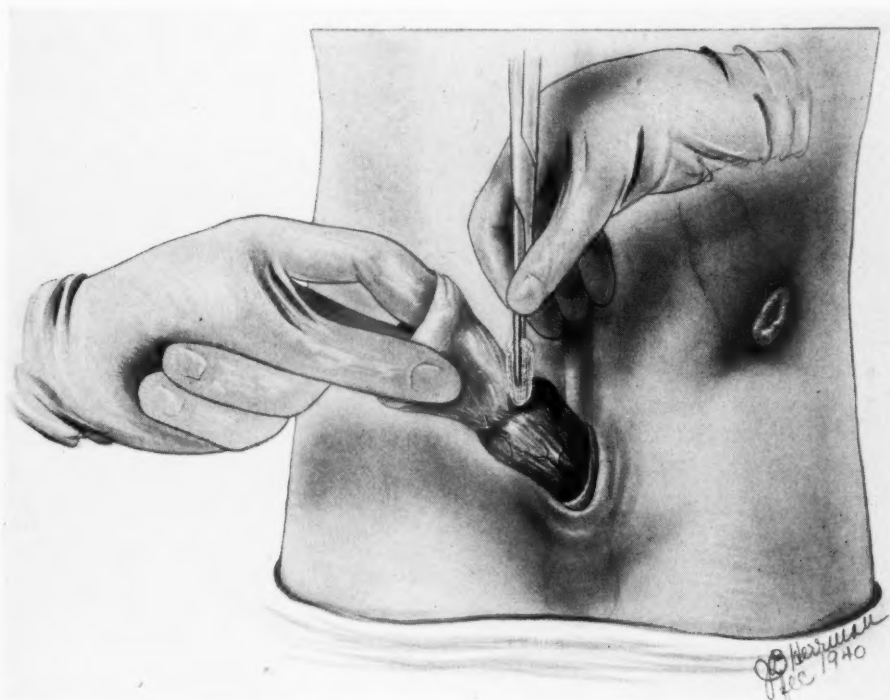


FIG. 3.—Second stage, or the mucosal-stripping operation. Usually performed two weeks or more after the first stage. Incision made about suprapubic colostomy. Mucous membrane identified and stripped out by pushing back muscular and peritoneal coats.



FIG. 4.—After all the mucous membrane possible, usually ten to 20 inches, has been stripped out above, a catheter is introduced into the sleeve of mucous membrane and fixed by suture.



FIG. 5.—Patient put in lithotomy position. Incision made about mucocutaneous junction of anus, and dissection of mucous membrane begun. Condylomata and fistulae, for the moment, are left alone.

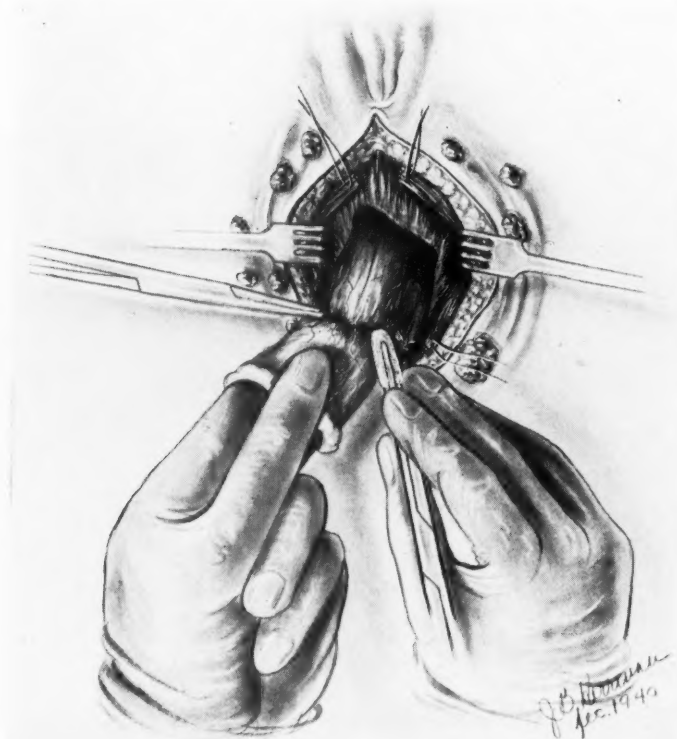


FIG. 6.—Mucous membrane being stripped out of rectum. Sphincters have been cut anteriorly and posteriorly, and retracted. Levator ani identified, and may be divided anteriorly and posteriorly if necessary.

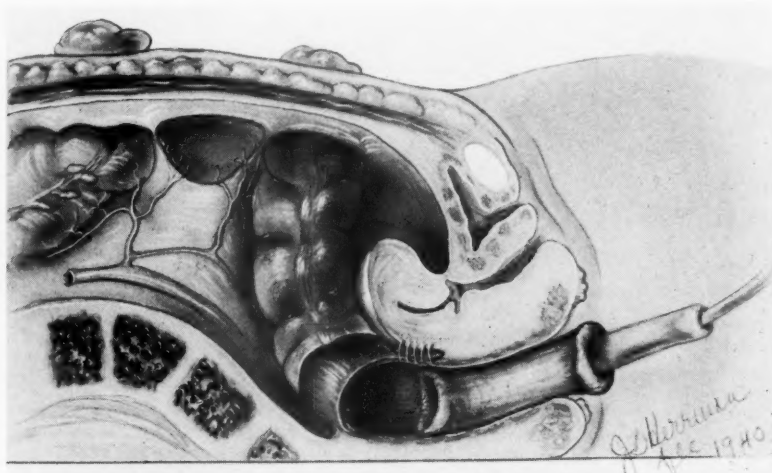


FIG. 7.—After the anal and lower rectal dissection has proceeded a few inches, the catheter tip in the rectum is grasped and pulled out through the anus, turning the sleeve of mucous membrane inside out. By further traction, and dissection if necessary, the whole sleeve of mucous membrane is delivered.

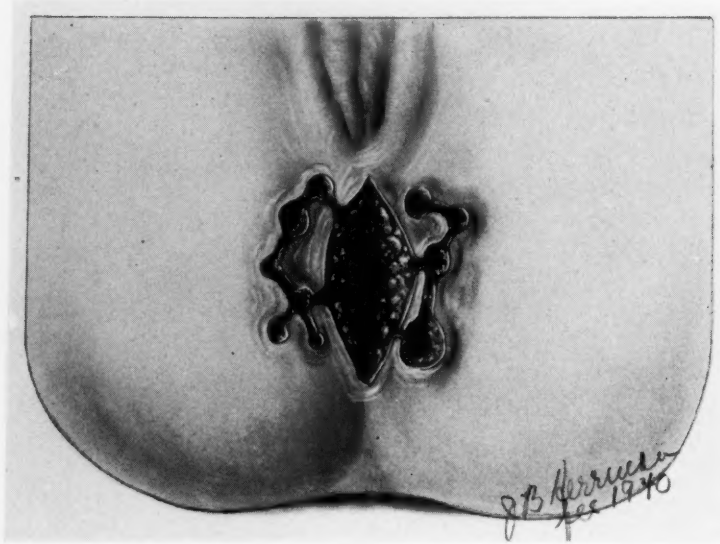


FIG. 8.—All fistulae are connected and opened wide. All condylomata are excised.

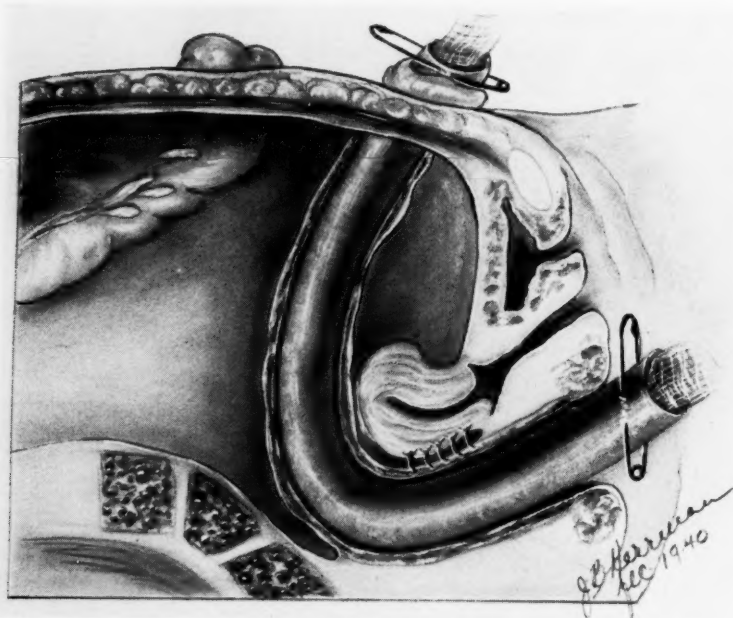


FIG. 9.—Drain left through from suprapubic to anal wound. The uterus is shown sutured to the rectal wall. This procedure of Warthen may be done at the first-stage operation if desired. It gives an added factor of safety in this disease.



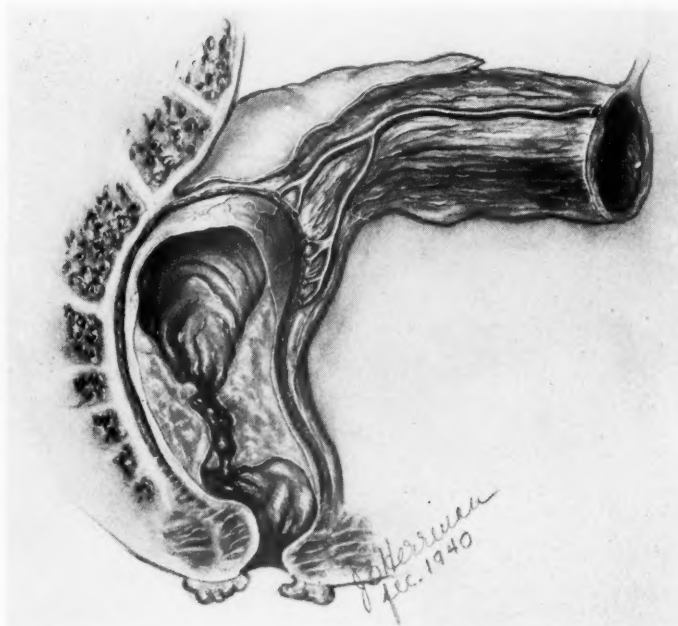


FIG. 10.—Showing that the blood vessels run between peritoneal and muscular coats. At intervals, small branches penetrate the muscle layer and then, after running along the submucosa, dip into the mucosa. The layers of bowel behind the stricture are easily identified because they are hypertrophied. Polypi, condylomata and fistulae are found below the stricture.



FIG. 11.—Twenty-three and one-half inch sleeve of mucosa and three condylomata stripped from Case 2 (C. B.).

very much like turning a coat sleeve inside out (Fig. 7). With further traction sometimes the whole mucosa may be entirely removed, even through the strictured area. We have, on all occasions, been able to do this in the cadaver (Fig. 12). If the mucosa cannot be stripped by traction through the strictured area, then some dissection may be necessary.

We next lay wide open all fistulae, and excise all of the surrounding skin condylomata (Fig. 8). Formerly we removed the fistulous and condylomatous areas in a single block, but we now find, as have others,<sup>12</sup> that when laid wide open, all these areas will entirely heal. Finally, sufficient drains are left



FIG. 12.—Mucosal-stripping specimen from the cadaver.



FIG. 13.—Roentgenogram of rectosigmoid in Case 1 (C. S.). The rectum was straight, contracted and fixed in heavy scar tissue.

through the dissected area from the abdominal wound to the perineal wound (Fig. 9). These drains may be entirely removed in about a week. The sinus thus left is irrigated twice daily with any solution desired. The wounds heal more rapidly than one would expect. The patient is discharged after two to three weeks, and returns to the clinic for dressings, or may be instructed to do them himself.

#### CASE REPORTS

**Case 1.**—C. S., white, male, age 56, was admitted to the Hospital for the Ruptured and Crippled March 14, 1932. For three years he had been suffering from rectal abscesses, fistulae, stricture of the rectum, and had had several operations. Examination showed an acutely ill man with a large perirectal abscess, stricture of the rectum, nine fistulous openings in an indurated ischio-rectal region, and a recto-urethral fistula through which feces and gas were passed. Roentgenologically, the bowel showed a narrow fixed rectum which looked like a pipe (Fig. 13). The Frei test was strongly positive. An immediate incision and drainage was done of the perirectal abscess. A suprapubic cystostomy cured his recto-urethral fistula. We dilated the rectum and opened fistulae on several occasions



FIG. 14.—Anal region of Case 1 (C. S.); four years postoperative. Before operation he had nine fistulae, many condylomata and sinuses, and a recto-urethral fistula.



FIG. 15.—Abdomen of Case 1 (C. S.); and Figure 14.

during the following year. Finally, on May 27, 1933, we established a colostomy of the first-stage Lahey type. The patient improved but the mucopurulent discharge from the lower segment was a source of great inconvenience to him, and required many dressings. The extent of the disease in the rectosigmoid made the complete excision of the rectum impossible. The problem was to, at least, get rid of the mucus. On October 14, 1936, in attempting to close the lower colostomy opening, so as to have all the discharge drain

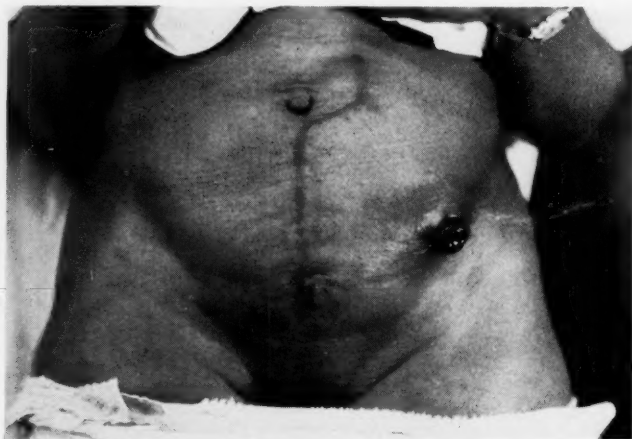


FIG. 16.—Abdomen of Case 2 (C. B.); operated upon 21 months previously. Clean, healed scar. Wears no colostomy bag.



FIG. 17.—Anal region of Case 2 (C. B.); 21 months after the second-stage operation. Before operation she had numerous condylomata, sinuses, rectal stricture, and great induration of the ischioanal region, with pus and bloody discharge, and partial intestinal obstruction.

at the anal end, we suddenly found that, after the mucosa was freed at the skin border, we were able to pull out and strip out some nine and one-half inches of the mucosa. We then placed the patient in the lithotomy position and, by a posterior incision through the densely scarred anus, we were able to dissect out what remained of the mucous membrane and rectal wall. The patient rapidly recovered and was discharged 15 days later. The large dressings, many times a day, were reduced in three weeks to a small piece of cotton

at the anal end night and morning. The patient has trained himself so that his bowels move every morning. He has now been well for four years (Figs. 14 and 15).

**Case 2.**—C. B., colored, female, age 35, was admitted to the Cornell Division at Bellevue Hospital, November 21, 1938, complaining of hemorrhoids, growth from the rectum, rectal bleeding and constipation during the previous two years. At examination we found the typical picture of a two-inch stricture of the rectum, beginning two inches inside the anus. At the anus there protruded a papillomatous growth. The whole ischio-rectal area was indurated and the seat of numerous condylomata and sinuses. Pus and blood was discharging from the rectum. The Frei test was strongly positive. On December 3, 1938, a colostomy was established and nine inches of sigmoid were removed. The condition of the patient greatly improved. On January 9, 1939, the mucosal-stripping operation was performed, 23½ inches of mucosa being removed (Fig. 11). The patient was discharged 22 days later. All wounds were healed in eight weeks and have remained so to date. Her bowels move once a day. She does not wear a colostomy bag (Figs. 16 and 17).

**Case 3.**—O. L., white, male, age 39, was first seen in Bellevue Hospital on December 30, 1938. He had lost 23 pounds in six months; he had rectal fistulae for 11 years, and had been operated upon at least five times in five different hospitals. Examination showed an emaciated man. The anal region was indurated, and distorted. There were nine fistulous openings, and the rectal mucous membrane was prolapsed. The Frei test was negative. On January 11, 1939, a colostomy was established and several inches of sigmoid removed. The patient's condition, generally and locally, improved. On February 28, 1939, the mucosal-stripping procedure was carried out, the entire tube of mucosa being relatively easily removed. The drain was removed in one week and the patient was allowed out of bed. In seven weeks the wounds were practically healed, the patient using a small piece of gauze at the anal end. The patient was heard of once since, and was said to be cured. We have not been able to get in touch with him further. This patient may or may not have been a case of lymphogranuloma venereum.

We have performed both stages of this operation on three other cases. The fourth and fifth cases returned to the clinic at Bellevue Hospital until they were about well. They then moved on from the Municipal Lodging House and have not returned to the clinic again.

**Case 6.**—J. A. G., colored, male, age 35, had the second stage of the operation August 23, 1940. He had a strongly positive Frei test, and a venereal history extending over 11 years. On admission to Bellevue Hospital he had a partial intestinal obstruction from stricture of the rectum, multiple condylomata, and 19 rectal fistulae. After the first-stage operation, June 19, 1940, he gained 12 pounds. The rectal mucosa was stripped out August 22, 1940. The condylomata were excised and the sinuses widely incised. Drains were all removed by the fifth postoperative day, after which time his temperature remained normal. The patient was discharged, 18 days after the second operation, in good physical condition, with almost negligible discharge from the anal region. All the sinuses were clean and healing rapidly. The intestinal tube was closed above and granulating well below.

We have four other cases upon whom we have performed the first stage of the operation. One has gone through a pregnancy. We have closed her colostomy twice, and on each occasion the local condition has become worse; the colostomy was opened once by nature and once by the surgeon. The other three have, thus far, refused the second stage of the operation. They improved immediately after their colostomies but the local condition is still very active, requiring a great deal of care and dressings. Another case had his colostomy



and, even with a negative biopsy report, was found, at the second operation, to have a carcinoma of the rectum in addition to lymphogranuloma venereum. We undertook an extensive excision of the rectum but the patient died one year later with metastases of the lungs, pleurae and kidneys.

COMMENT.—We have pathologic reports on all of our cases, but we have not presented them and their photomicrographs here because it is the feeling of our pathologists at Bellevue Hospital, and of others,<sup>18</sup> that a diagnosis cannot be made from a tissue examination. The latter is of help in excluding other diseases, such as syphilis, tuberculosis and carcinoma. The tissue reports are always similar: Acute and chronic inflammation, submucosal fibrosis; muscular hypertrophy; dense lymphocytic infiltration; necrosis; mucosal polypi; *etc.* However, tuberculosis, syphilis and carcinoma are so frequently associated with this disease, that roentgenograms of the chest, blood Wassermann tests, the Frei test, and a biopsy should always be done. Greenblatt,<sup>19</sup> in a recent article, has drawn attention to the frequency with which genital and rectal malignancy is clothed in the guise of a venereal disease.

Because the medical profession is not yet fully aware of the inadequacy of ordinary treatment of this disease, all the authors of recent articles, on the surgical treatment, have emphasized that some cases are refractory, the prognosis is bad, a systemic spread may occur, and death from sepsis, peritonitis, and cachexia happens more often than is generally recognized. A simple colostomy is a tremendous relief to these patients, and it will prolong life many years, but cases are being reported,<sup>12</sup> and we have seen two such cases, where the disease had extended up the sigmoid and had actually involved the colostomy stoma. We also see a few cases every year who have had a colostomy performed elsewhere and whose symptoms, locally, have increased until they are admitted to our hospital wards for further treatment. Another interesting point is the number of years a patient can go with almost complete intestinal obstruction from the stricture. We have had several cases go for three or four years with strictures through which we could not pass a small bougie. Finally, they would submit to colostomy.

The reaction after the mucosal-stripping operation is not severe. The temperature rarely rises more than two or three degrees. The patients are often anemic and need a blood transfusion. We have, thus far, only operated upon the worst type of cases with the anorectal syndrome. Out of six cases we have not had a fatality. One case with multiple fistulae and an 11-year history without a positive Frei test, was submitted to the operation and greatly benefited by it. We believe, therefore, that the operation may be indicated in certain cases of multiple fistulae, especially where the sphincter has been irreparably damaged. We offer this report as a preliminary one, and we realize that six cases are not sufficient to prove the value of the operation. We do feel, however, that the mucosal-stripping is a new idea. We would like to offer it for what it is worth. It does have the advantage of not entering the peritoneal cavity, and avoiding the consequences which may thus follow in these infected cases.

CONCLUSIONS

(1) An operative procedure for the anorectal type of lymphogranuloma venereum is described. The second stage consists of stripping the mucosa from the layers of the lower sigmoid and rectum—which we believe to be a new feature.

(2) Five cases, thus far treated, have been greatly benefited.

(3) One case of multiple rectal fistulae, not due to lymphogranuloma venereum, has been improved by this operation.

(4) We believe the operation deserves a further trial on such cases.

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DISCUSSION.—DR. JOHN H. MORRIS (New York) said: Lymphogranuloma inguinale has been gradually assuming a more prominent place in present-day literature and there is certainly a notable increase in the number of reported cases. Whether this increase is relative or absolute cannot be stated but it does appear probable that reclassification of rectal strictures with the consequent frequent elimination of the diagnosis of syphilis and gonorrhea may be held to account for the fact at least in some degree.

In any event, the treatment of this increasing group of cases has become a pressing problem particularly since the therapeutic approach to this disease—whether medical or surgical—has not been satisfactorily established. Reports from various sources indicate the success of conservative measures of treatment comprising the use of sulfanilamide, roentgenotherapy, diathermy, *etc.*, and there can be no doubt that many of these cases respond to such measures.

It is equally true, however, that an undetermined percentage of these cases—and particularly the type seen in the city hospitals—present a group of serious complications such as periproctitis, abscesses, strictures and fistulae. While the disease itself may respond to conservative measures, it is certain that those complications incident to it definitely demand radical surgical therapy.

It is significant that the type of surgical therapy best adapted to this condition is also not definitely established. Colostomy or colostomy plus complementary operation has been the main objective but it is to be noted that these colostomies are usually permanent and that they must be established in young patients. The ideal procedure is unquestionably that which removes a progressive lesion and restores the continuity of the intestinal tract, thus avoiding permanent colostomy. This ideal is not always attainable, however, and, therefore, the ingenious procedure described by Doctor Patterson merits consideration because of the satisfactory after-results and the unusually low mortality possibilities. In this connection it is interesting and significant to note that the progress of this disease seems to have been stayed by an attack upon the mucosa alone. There has been a general belief that the virus of this disease is spread via lymphatic channels and intramural extension. The response in Doctor Patterson's cases, if confirmed by longer observation, may well contribute valuable information to the etiology of lymphogranuloma venereum.

In view of the different types of surgical approach to this disease, Doctor Morris showed a case in which resection of the involved rectum was carried out, the intestinal canal reestablished, and a satisfactory sphincteric control accomplished.

**Case Report.**—A Negress, age 31, was admitted to the Fourth Surgical Division of Bellevue on January 31, 1940, with a diagnosis from another hospital of acute perirectal abscess, multiple fistulae, stricture of the rectum, and a rectovaginal fistula. The Frei test was reported as positive from this other hospital.

Her illness dated back five years. The onset of the stricture began with small fecal movements that were very difficult and painful. Shortly thereafter she developed an abscess about the rectum which ruptured spontaneously. This was followed by profuse purulent discharge and fistula formation.

Five weeks before admission she consulted a physician who advised and carried out operation for the fistula. Thereafter she began to discharge pus and fecal matter from the vagina, while there was considerable bleeding from the rectum. For the succeeding four weeks she was treated by daily irrigations and packing. She was then advised that nothing further could be done for her condition.

Examination on admission revealed to the left of the anus an indurated sinus tract discharging pus profusely, and leading high up into the hollow of the sacrum. There seemed to be no discharge coming from the rectum. The entire perianal region was indurated, tender and swollen. On rectal examination an inflamed anal stricture barely admitted the tip of the index finger three inches from the anal margin.

Vaginal examination disclosed no evidence of rectovaginal fistula but an extensive, hard, tender mass could be palpated through the posterior vaginal wall. Laboratory data;

2,200,000 red blood cells, 18,000 white blood cells, 92 per cent polys. Blood Wassermann negative. Frei test positive.

During the succeeding three weeks under observation the patient ran a persistent, intermittent type of temperature with a daily maximum of 104°-106° F., and she became quite toxic. The abscess about the rectum continued to drain through the vagina. Vaginal examination showed the pelvis to be negative, but she continued to have the extensive perirectal mass. Conservative treatment in the form of transfusions, glucose, sulfanilamide, *etc.*, were carried out without demonstrable improvement. In view of the progressive toxemia, it was decided that some surgical attack should be attempted.

Accordingly, on February 2, 1940, a proximal short-circuit of the bowel was effected by means of a Devine colostomy at the level of the hepatic flexure. The general and local condition improved markedly. The patient was discharged one month after operation, with instructions for daily irrigation of the distal isolated loop.

On readmission, the diagnosis of stricture was unchanged, but the discharge from the fistula had decreased, and the perirectal abscess had improved to some degree. On May 11, 1940, the following procedure was carried out:

A curved transverse incision was made from one ischial tuberosity to the other, with its concavity toward the rectum. Dissection was carried upwards through the perineum between the rectum and vagina until the cul-de-sac of Douglas was encountered. The peritoneal cavity was opened so that an uninvolved segment of bowel could be secured and the bowel was sectioned high up. The distal segment was freed down to a point proximal to the external sphincter where it was again sectioned and the involved segment with stricture and thick-walled rectum removed. The proximal cut-end of uninvolved bowel was then brought through the external sphincter, which had previously been denuded of its mucous membrane, after the Whitehead method, and sutured to the skin edges. The wound was closed with drains in either angle of transverse wound.

A satisfactory recovery was obtained, and one month after the above resection the spur of the Devine colostomy was crushed and the fecal current reestablished.

In the meantime rectal dilatation had been carried out at regular intervals and the Devine stoma was subsequently closed, under local anesthesia. Her present status is that colostomy wound and perineal wounds are both well healed. There is no rectal stricture or fistula, no recurrence of granulomatous process, and bowel movements are normal and well controlled.

This operation was originally described by Pochet, in France, and has been carried out successfully in this country by Dr. Louis Wright at Harlem Hospital.

DR. RALPH COLP (New York) stressed the fact that lymphogranuloma venereum is becoming a real problem in the New York area because of the great increase in the Porto Rican and Negro population. It is a serious, progressive, debilitating type of disease which leads to chronic invalidism, and the treatment of which should be based fundamentally upon its pathology. It is probably due to a filtrable virus. While it might start in the rectum as a local lesion following pederasty, this is not the usual path by which the rectum and sigmoid are involved. It invariably involves the nodes of the femoral and iliac region with a cicatrization of the endopelvic fascia which results in lymph stases, producing an edema of the mucous membrane of the rectum. This, abetted by the passage of the fecal content, causes a progressive ulceration of the mucous membrane with a seropurulent discharge, ending eventually in stenosis of the rectum. When these lesions begin, they should be treated energetically by medical means, and some good results have been obtained from chemotherapy and the injection of the Frei antigen. However, if the disease shows a tendency to progress, surgery should be resorted to. As Doctor Patterson has stated, dilatation of the strictures is of little avail. In Doctor Colp's experience, the results following the removal of the fibrous connective tissue about the rectum, from a posterior sacral approach, have

not been successful. Bearing the pathology in mind, the ideal procedure would be an excision of the diseased area of rectum and rectosigmoid, together with the nodes which were really responsible for the lesion. In 1925, Villard and Rickard recommended an abdomino-endo-anal resection of the rectum and rectosigmoid for carcinoma, mobilizing the sigmoid, and reimplanting it through the anal sphincters. In selected cases, this procedure, which entails a high mortality, has been employed a great deal for granuloma venereum in South America. Doctor Colp said he had employed it twice, with an excellent functional result in one case and a poor result in the other. These cases were operated upon three years ago and both are well and have had no signs of a recurrence of their disease. A more logical procedure is that advocated by Kindall and Edwards who, in 1923, advised a loop-colostomy which will divert fecal content, followed by a perineal resection of the diseased rectum and sigmoid. The reason that this procedure is a good one is that it removes the actual diseased node, and the diseased area of the bowel. Doctor Colp could not agree with Doctor Patterson that loop-colostomy *per se* may be followed by an extension of the disease in the proximal bowel. This disease probably does not spread by continuity, but the ulcerations of the mucous membrane are secondary to lymph node involvement. There are cases, however, which, because of extensive fistulization of the perineum, will not tolerate resection, and it is in this type of case that the procedure contributed by Doctor Patterson is especially indicated. The "stripping" operation rids the patient of an annoying discharge and makes his life fairly comfortable. Whether these patients will have a further extension of the disease, only time will tell. The idea is well-conceived as a palliative procedure and should certainly be tried in those cases which are truly inoperable from the standpoint of a loop-colostomy and perineal resection.

DR. W. HOWARD BARBER (New York) said that observations made upon the Third Division at Bellevue Hospital correspond in most respects with those of Doctor Patterson. There is a decrease in the total number of rectal lymphogranulomata admitted on the Surgical wards. This is probably due to more effective medical treatment of the constitutional aspects of lymphogranuloma venereum. A small proportion of these refractory cases continue to resist all forms of nonsurgical therapy and develop rectal stenoses and strictures, ulcerative proctocolitis, and extensive regional lymphadenitis. If these cases are not arrested by surgical means they terminate fatally by intestinal obstruction, profound toxemia and asthenia, perforation of the colon and peritonitis, or metastases and septicemia. The means of progression from the most frequent primary venereal sore is by the lymphatics to the rectal and perirectal tissues, to the regional nodes of the rectum and sigmoid, and in the extreme cases to the preaortic lymphatics and to the nodes behind the transverse mesocolon. In rare instances the virus appears to be carried by the venous blood, particularly through the superior hemorrhoidal and inferior mesenteric vessels, to the portal vein and liver. The granulomatous process may extend directly along the bowel wall but rarely above the splenic flexure, and the manner of such extension is not clear. The progression may be through the lymphatics of the bowel wall and the ulcerative colitis due to a secondary infection. In view of these observations the paramount indications for surgery are taken to be: (1) Relief of intestinal obstruction; (2) ablation of the chief pathologic site of the disease; and (3) interruption of the spread of the disease within the abdomen. These are thought best met by: (1) An abdominal colostomy; and (2) sacroperineal resection of the rectosigmoid together with the involved pararectal and presacral lymphatics. The



results of this program in our wards have been followed by a striking improvement in the weight and well-being of the cases operated upon and a mortality of 14.3 per cent for the first 35 resections.

Doctor Patterson has presented a very interesting thesis on the stripping of the mucosa from the rectosigmoid and resection of the anorectum, following a preliminary abdominal colostomy. This is applicable in those cases wherein the mucosal lining is not too involved to be separated from the remaining rectal wall and above the stricture. Excision of the remaining stenosed rectum and anus eliminates a considerable portion of the most diseased tissues.

Doctor Morris' case of rectal resection with preservation of the anal sphincter for control of a perineal colostomy has been well executed by him. Such procedures have been reported by Colp and others with varying success. Our experiences with anal plastics have led us to avoid them. In the interest of more complete eradication of the diseased bowel we prefer to produce sacral colostomies where it is possible or desirable.

DR. RUSSEL H. PATTERSON (New York) said, in conclusion, that the patient had had his colostomy in 1932. The mucosal-stripping operation was performed in 1934. It has now been six years and the patient has gained 30 pounds in weight and is up and about at his business every day. One case shown tonight had the mucosal-stripping procedure carried out only a few weeks ago. The case was presented to demonstrate how the healing process takes place. The second patient had the mucosal-stripping procedure carried out one year ago. She has had no symptoms or signs of a recurrence of her trouble.

In response to Doctor Colp's mention of the mode of acquisition of the anorectal type of this disease, Doctor Patterson said he had purposely avoided this controversial phase of the subject. There are two main schools of thought as to mode of acquisition. One school believes that the virus comes in contact with the mucous membranes of the genitalia and spreads to the inguinal nodes and eventually to the pelvic nodes and the perirectal tissues. The other school believes that the virus is deposited directly on the rectal mucous membrane, as the result of pederasty, an acute proctitis results, and eventually a stricture of the rectum. Doctor Patterson said he leaned toward the belief of the latter school. Doctor Arthur Grace of the New York Hospital, in examining some 200 cases, obtained a positive history of pederasty from 80 per cent of the male patients.

Doctor Patterson expressed the opinion that the procedure described by Doctor Morris in the case he showed is excellent for rectal strictures that are uncomplicated by sinuses and infection. Doctor Patterson said he had been encouraged in the one case upon whom he had operated in a similar way. Simple colostomy does help a great many of these patients. However, Doctor Patterson felt more radical surgery is needed in the severe cases such as those described in his paper.

## ENDOMETRIOSIS—ITS SIGNIFICANCE\*

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IN AUGUST, 1938, in an editorial,<sup>3</sup> attention was drawn to the fact that endometriosis was increasing in frequency and that there was probably some reason for it. It was felt that the increase might be due to delayed marriages and to lack of early and frequent child-bearing, and suggested that the economic difficulties of the day were responsible for the increased frequency.

Since that writing, all cases in my private practice have been very carefully explored, and any piece of tissue suggestive of endometriosis has been excised and fixed in Zenker's solution before the removal of any organ was begun. Probably, the fact that pieces of tissue have been separately removed and preserved, is partly responsible for the finding of increased numbers of this lesion. It is also probable that because of the great increase in total hysterectomies, with a wide exposure of the posterior cul-de-sac and the uterosacral ligaments, more small posterior lesions have been found. The high percentage of positive microscopic findings and the greater percentage of gross findings have led to the conclusion that endometriosis is brought about by a physiologic response to persistent and uninterrupted menstruation. Something (estrin?) stimulates the celomic epithelium and this stimulation causes the epithelium to attempt to produce small areas of endometrial tissue, endosalpingial tissue, or even endocervical tissue. So great is the concern about this lesion and its frequency, with its definite lowering of fertility, that patients with stigma of lowered fertility are urged to marry and bear children early. Normal girls over 23 are urged to have a child as soon as possible after marriage. Many men and women cannot afford to be burdened with children immediately after marriage; but as youth is the proper time to have children it is right that they be urged to do so. Dr. Thomas R. Goethals, of Boston, found that in 75 per cent of 200 private primiparae the average age at the birth of the first child was 28 years. All this fits into the theory that an apparent increase in this entity is due to the economic difficulties of our times. Sampson,<sup>7</sup> in 1924, reported 64 instances in 296 celiotomies, or 21.6 per cent, and, in 1925,<sup>8</sup> 98 out of 332, or 29.5 per cent—a total of 162 out of 628, or 25.7 per cent. These statistics of Doctor Sampson are high; but it must be remembered that at that time, because of his work with endometriosis, patients from everywhere, who were suspected of having the disease, were being sent to him. This, I believe, has something to do with the figures presented. The cases described in this article were sent because of varied pelvic pathology; and none were suspected of having endometriosis.

\* Read before the American Surgical Association, White Sulphur Springs, W. Va., April 28-30, 1941.

*Definition.*—There are two main types of ectopic endometrium: In one, and this does not figure in this communication, the endometrium is found growing down from the endometrium into the myometrium. It may invade the myometrium very deeply, but usually is made up of a few glands growing away from the normal lining of the uterus; occasionally, the growth penetrates the entire uterus, and may even invade incidental fibroids that are present. This lesion is known as adenomyoma or adenomyosis.

The second type, and the one that is being discussed here, is made up of areas of ectopic endometrium, either in the ovary, tube, pelvic peritoneum, on the front of the uterus, or in the uterosacral ligament, *etc.* The lesion may be widespread and the whole pelvis bound down by adhesions, or there may be a spot no larger than the head of a pin. The area may be blue, black, or purple, or there may simply be a pucker in the otherwise smooth pelvic peritoneum. Sections of this tissue will show glands similar to endometrial glands and a stroma similar to endometrial stroma. This tissue may respond to the stimulation of estrin to produce the growth phase, or to progesterin to produce the secretory phase, or to pregnancy to produce decidua in the stroma; but just as the basal layer of the normal endometrium does not react to any ovarian stimulus, so also this tumor may not. However, enough cases have been seen that respond to ovarian stimulation, and that are so very like endometrium in microscopic appearance, that it is fair to assume that they are one and the same thing. I doubt if anyone questions, now, that the endometrium of endometriosis is not similar to normal uterine endometrium.

*Theories for Development.*—Cullen,<sup>1</sup> long ago, showed that the first type of endometrioma, the adenomyoma, is a down-growth from the endometrium, and that the glands are often connected with the endometrium. In a series published<sup>2</sup> from the Massachusetts General Hospital, in 1934, it was definitely shown that this lesion was more frequently present in women who had had multiple pregnancies. This is due, perhaps, to the growth and involution of the uterus and the activity of the endometrium as it passes through numerous pregnancies. Perhaps small pieces of tissue are caught in the myometrium when the changes take place.

Sampson postulated the idea that endometriosis is due to two possibilities: One, that the endometrium during a normal menstrual period may be swept in a backward direction and flow into the peritoneal cavity and attach itself and grow upon or into any pelvic organ; two, that an ovarian endometrioma may menstruate, swell, and rupture, and in rupturing spread endometrium that is viable into the pelvis, or itself become attached to the peritoneum and grow and invade it. This study cannot refute this theory, nor does it attempt to do so. In nearly every one of our cases the tubes were patent—a proof that reflux could take place. All of us have seen reflux bleeding during a period. The many years of uninterrupted menstruation in these cases would seem to give greater chances for the endometrium to flow through and grow. If, however, the menstrual flow is due to sloughing off of tissue that has become anoxic (a current theory of menstruation) I think that it is unlikely that the tissue

that comes through the tube would be viable. Nature certainly did not intend that reflux bleeding should be responsible for the growth of invasive tissue in the pelvis. Menstruation itself may be a kind of abnormality, for it occurs only infrequently in monkeys in their natural habitat.

The theory of lymphatic extension, that is metastasis of endometrium through the lymphatics, probably is not the correct method of its spread. However, many very able men believe in this theory.

Iwanoff and Meyer<sup>4</sup> have proposed that inasmuch as the plevic peritoneum is the celomic epithelium, and as the celomic epithelium is the original source of the endocervix, endosalpinx, and endometrium, this tissue may still contain groups of viable embryonic cells, and under certain conditions they may grow, and in growing reproduce what they produced in the embryo. It is thus possible that just as the endometrium and endosalpinx and endocervix respond to estrin and progestin by growth and function the pelvic peritoneum (celomic epithelium) may grow and produce if the stimulation is constant and not interrupted, as it should be, by pregnancy. Interruption of the menstrual cycle by pregnancy is a physiologic change in women. When it is realized that the frequency of endometriosis in patients with stigma of underdevelopment is twice as great as in those without it, this theory is even more tenable, for patients with underdevelopment may have more left-over cells. If pregnancy is a check upon the development of endometriosis, and I believe it is, what is there in pregnant women that checks the celomic epithelium from growing? Certainly estrin and progestin are produced in greater quantities during the pregnant than in the nonpregnant state. This normal physiologic process, although perhaps not preventing it, must have something to do with avoiding endometriosis. It is probable that this theory is the correct one, namely, that epithelium which originally grew endometrium can, under certain abnormal conditions, again produce cells capable of becoming endometrial tissue.

*Symptoms, Diagnosis, and Treatment.*—These have been described so many times that this paragraph will be brief. The symptom occurring most frequently is that of acquired dysmenorrhea, which is usually accompanied by a change (increase in the amount) of the menstrual flow. The physical diagnosis is not difficult in a patient over 29 years of age, who presents symptoms of pelvic inflammation, who has had no children, and who, on vaginal or rectal examination, has a moderately fixed pelvis, with a rough or shotty feeling in the posterior cul-de-sac. Such findings may be interpreted as the result of endometriosis. The treatment may be radical or conservative, depending upon the age of the patient, the extent of the disease, and the patient's desire for children. Occasionally, bilateral oophorectomy will be necessary. Roentgen therapy destroys ovarian function, and this is followed by atrophy of the endometriosis as well as atrophy of the normal endometrium. Therefore, one can be conservative when it is deemed best. In older women, radical surgery is best if it can be undertaken without danger to the life of the patient. This tumor can be very difficult to remove, and injury to the rectum, bladder, uterus, or intestines can occur. At operation, it is frequently noticed that the uterus is flexed backward upon itself, the fundus and cervix being

attached to one another, the uterosacral ligaments are obliterated, and the posterior cul-de-sac drawn up on back of the bent uterus. This must be recognized during operation, as perforations of the rectum or incomplete surgery may otherwise result. When the uterus is straightened out and the cul-de-sac freed, a very wide, raw area will be found on the posterior wall of the uterus and in the cul-de-sac of Douglas. This is definite evidence of abnormal development and endometriosis is often recovered from these areas. The uterosacral ligaments may be missing following release of the uterus and cul-de-sac.

*Increased Frequency.*—The increased frequency may be actual, or it may be due to more careful observation and better exposure of the cul-de-sac and uterosacral ligaments. But there is probably more to it than that, for during my apprenticeship with the late Drs. W. P. Graves and G. W. W. Brewster, from 1921 to 1927, search was made for these lesions because of the great interest aroused by Doctor Sampson's observations. Yet not a great number of lesions were found. That is probably because the patients operated upon, then, were married earlier and bore children earlier than those who have been operated upon during the last four to five years. It is probably true that our mothers and grandmothers married early and had many children, and that they rarely had this abnormal physiologic process. There is no doubt that great interest stimulates more careful search. The habit of placing sutures about the areas, or placing safety-pins under them, or even excising the areas has been developed. In the early cases in this group, numerous areas of endometriosis were missed in the laboratory, for a blood-covered uterus is not the easiest place to find the fine, blue to purplish spots that represent this growth. Doctor Tracy B. Mallory, the Pathologist at the Massachusetts General Hospital, has admitted that my diagnosis, in the gross, is probably as correct as his by microscope; and if that is so, then the number is even greater than the histologic findings would indicate. I have been a student of this lesion since Doctor Sampson first drew attention to it, and I have worked and puzzled about it for years.

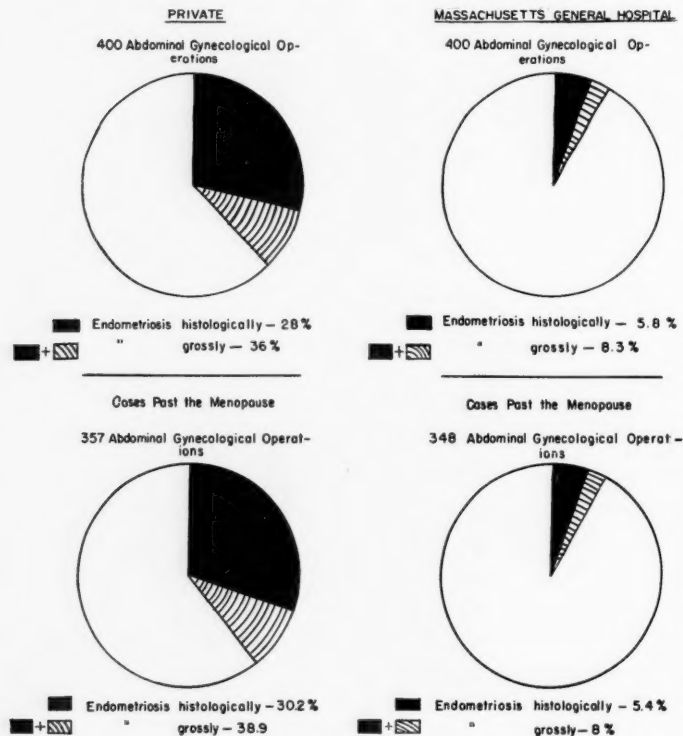
I believe that the theory of Iwanoff and Meyer is the correct one, and that the great frequency of endometriosis, as reported in this communication, is due to careful observation and the removal of pieces of tissue, but that the real reason for the frequency is that endometriomata are not tumors but represent abnormal physiology due to late marriage and delayed and infrequent child-bearing. The latter is due to the economic times we live in, and my plea is that patients with apparent infertility, evidences of underdevelopment, and older girls about to be married, be taught how to become pregnant and not how to avoid pregnancy, even though their finances are limited. The monkey mates as soon as she becomes of age, and has offspring until she can no longer have any or until she dies. Menstruation in this animal must be rare. As women have the same physiology it must be wrong to put off child-bearing until 14 to 20 years of menstrual life have passed. During a prolonged, uninterrupted menstrual career changes in the celomic epithelium from whence the endo-



metrium originally came must take place. Endometriomata are not true tumors but are areas of growth due to abnormal physiology. Another important finding is the comparison of private patients, most of them fairly well-to-do, to a similar group of patients at the Massachusetts General Hospital. The hospital patients are of that social status that marries early and has children frequently, and in this group there are fewer cases of endometriosis. Their more normal functions are reflected in the small incidence of endometriosis.

TABLE I

	Private	M. G. H.
Abdominal gynecologic operations.....	400	400
Histologic endometriosis.....	112-28%	23-5.8%
Gross endometriosis.....	144-36%	33-8.3%
Abdominal gynecologic operations Excluding cases past the menopause.....	357	348
Histologic endometriosis.....	108-30.2%	19-5.4%
Gross endometriosis.....	139-38.9%	28-8%



Diagrammatic representation of Table I.

*The Material.*—The last 400 consecutive abdominal gynecologic operations in my private practice were analyzed very carefully, and certain important findings noted. Four hundred consecutive patients who had had abdominal gynecologic operations at the Massachusetts General Hospital were studied to find the percentage of endometriosis to compare with the private group. In

# ENDOMETRIOSIS

the group of patients who came to my office, and were operated upon by me, 112, or 28 per cent, showed microscopic evidence of endometriosis, as against 5.8 per cent in the Massachusetts General Hospital group. The number of patients who were considered, grossly, to have endometriosis at operation was 144, or 36 per cent (Table I).

These patients were not, in many instances, suspected of having endometriosis before operation, and in many instances the endometrioma consisted of a very small isolated area. The point is, however, that they had what we understand as endometriosis, and it might easily have grown larger if let alone. The process was there, though not giving any symptoms.

A comparison was then made between the endometriosis group and the rest of the 400 who did not have endometriosis. In the endometriosis group, 74.1 per cent were married, and of the others, 74.3 per cent were married. In the endometriosis group, 53.1 per cent were over 25 when married, and in the other group, 57.3 per cent. These statistics are, so far, all nearly identical. But the fertility in the endometriosis group was 65.7 per cent, while in the other group it was 83.3 per cent (Table II). This latter figure for fertility is

TABLE II  
400 ABDOMINAL GYNECOLOGIC OPERATIONS (PRIVATE)

	Endometriosis	No Endometriosis
Married.....	74.1%	74.3%
25 years of age or over at marriage.....	53.1%	57.3%
Two children or less.....	73.4%	49.3%
Fertility of married group.....	65.7%	83.3%
Stigma of underdevelopment.....	27.6%	15%
Marriage to first pregnancy over two years.....	66%	66.6%
Age at first pregnancy, 25 or over.....	63.4%	
Age at onset of symptoms, over 27 years.....	108 cases	
Menarche to endometriosis, 17 or more years.....	105 cases	
Number of years from menarche to first pregnancy 11 or more years.....	73%	
Age of patients with endometriosis over 29 years.....	All but one	

too low, but this is not unexpected, as most of the patients were operated upon for fibroids, cancer, bleeding, ovarian tumors, *etc.*, so that they also must have a lowered fertility. Reynolds and Macomber,<sup>5</sup> in their book on Fertility and Sterility, give 88 per cent as normal fertility in the married. Congenital erosions (exposure of the endocervix), very painful breasts, narrow pelvis, severe dysmenorrhea, juvenile uteri (measured), and infrequent periods were considered as stigma of underdevelopment. The endometriosis group had 27.6 per cent of patients with evidences of underdevelopment, while in the other group there were but 15 per cent. The endometriosis group, therefore, showed nearly twice as many patients with underdevelopment. Seventy-three and four-tenths per cent of the patients with endometriosis had two or less children, whereas in the other group 50.7 per cent had over two children. Sixty-nine per cent of the endometriosis group did not have the first child until two or more years after marriage, and of the other group 66.6 per cent did not. Other statistics of interest are as follows: For the group with endometriosis, the age at the first pregnancy was 25 or over in over 63.4 per cent; the age of the onset of symptoms was over 27 in 108 of 112 patients. The age of patients

with endometriosis, when it was found, was over 29, in all but one patient. The number of years from the onset of periods to the finding of endometriosis was 17 years or more in 105 out of 112 patients. In 57.4 per cent of the endometriosis group there was a change in the patient's characteristic menstrual flow. The preoperative diagnosis was made correctly in 41 per cent of patients. Endometriosis was found in the ovary in 57.1 per cent, on the peritoneal surface in 51.6 per cent, and in 18.7 per cent its location was the uterosacral ligament. In 32.1 per cent of patients dysmenorrhea was a complaint; 33 per cent complained of pain other than dysmenorrhea; 23 per cent had urinary difficulty; and 28.6 per cent had bowel habit changes. There were 85.7 per cent who had a radical operation, that is hysterectomy with or without removal of the ovaries, and but 14.3 per cent had conservative surgery. Three patients with conservative surgery had children following operation (Table III).

TABLE III

Region of Endometriosis	
Ovary.....	57.1%
Peritoneum.....	51.6%
Uterosacral ligament.....	18.7%
Operation	
Radical.....	85.7%
Conservative.....	14.3%
Symptoms	
Dysmenorrhea.....	32.1%
Pain other than dysmenorrhea.....	33%
Urinary symptoms.....	23.2%
Change in catamenia.....	57.4%
Bowel symptoms.....	28.6%

## CONCLUSIONS

- (1) Delayed marriage, delayed and infrequent child-bearing all contribute to an increase noted in endometriosis.
- (2) Less well-to-do patients in a general hospital population have less endometriosis than patients in private practice.
- (3) Stigma of underdevelopment means lowered fertility and greater incidence of endometriosis.
- (4) The celomic epithelium or pelvic peritoneum may be stimulated to produce endometriosis (Iwanoff and Meyer).
- (5) Modern economic trends are responsible for delayed marriage.
- (6) Young married couples should be urged to have children early, and practice contraception after they have their families. They should be taught how to have children, not to avoid them.
- (7) Financial aid from parents in the early years of marriage should be offered and welcomed when possible.

The significance of endometriosis is that it is a stigma of infertility, and it is due to uninterrupted menstrual cycles, because of late marriage and infrequent child-bearing. Therefore, as it is increasing in private practice among those having children late in life and few in number, it is better for us, as doctors and fathers, to urge early marriage and early and frequent child-bearing.

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DISCUSSION.—DR. JAMES C. MASSON (Rochester, Minn.): Doctor Meigs' paper is on one of the subjects that are foremost in the minds of gynecologists at present, and there is no doubt that those who are "endometriosis-minded" find this condition frequently, whereas the general surgeons, and those who are not especially interested in the subject, see it rather rarely. I was impressed by the carefully prepared and convincing statistics of the essayist. There is no doubt that the condition is recognized more frequently than formerly, and the reason for this is probably that a real interest in the subject was stimulated by Sampson's paper about 20 years ago. Since that time, operations have become more frequent, especially more radical operations including total hysterectomy, and the more frequent examination of tissue removed has been, as suggested by Doctor Meigs, a factor in the more frequent recognition of the condition.

The possibility of delayed marriage, and of delayed child-bearing, has to be considered, but in this connection I would like to note that 50 per cent of the patients in my series were married before they were 24 years of age. I am sorry that I cannot give the dates when their first babies were born. In one case, endometriosis was diagnosed one year after the onset of the menstrual periods.

In one case, I reported to this Society in 1935, when I presented a paper on this subject, the patient had rather extensive endometriosis, in which the only serious lesion, I feel, was the one on the sigmoid. It was a benign tumor, but might grow sufficiently to cause obstruction. Another very important condition in this case was an adenomyoma in the rectovaginal septum. The "endometriosis-minded" surgeon frequently sees small implants in the cul-de-sac, on an ovary, or on the uterosacral ligaments. Many of them, I think, never cause serious trouble and, unless the tubes are occluded, pregnancy is still possible.

It is my impression that a great many of the smaller endometrial implants suggest, very strongly, Sampson's idea of a reversal of the flow of the menstrual fluid. I think a great many of them eventually disappear. I want you to keep in mind this picture, and I will refer later to large, tarry cysts and endometrial tumors in ectopic positions.

I want to draw attention to the number of cases in which endometriosis was located in the uterus in my series. In 482 of 576 cases encountered, the adenomyomata were in the uterus. A great many of these were diffuse adenomyosis of the uterus, but there were numerous implants on the visceral peritoneum. In 14 cases, endometrial implants were on the sigmoid, in 20 cases, in the rectovaginal septum, and in 77 cases, in the ovary. Some were huge, tarry cysts. In recent statistics, the number of large tumors or cysts remain about the same but there is a great increase in the smaller implants.

If persistent and uninterrupted menstrual periods have a marked influence on this condition, then I would think that a younger married woman would have to have many children to protect her until the time of her menopause. If she had two, three, or four children early, and then started contraceptive methods, she would have a long period of

constant and uninterrupted menstrual periods and, if Doctor Meigs' theory is correct, endometriosis might develop later in life.

Doctor Meigs has made a strong case for the hormonal influence of estrin on the columnar epithelium, as suggested by Meyer. In 1935, in speaking on this subject before this Society, I expressed the opinion that many of the tumors which are similar, microscopically, may have different origins, and I still believe it. Besides the stimulation of the columnar epithelium, I think the possibility of embryonic rests being stimulated in the same way and the occasional possibility of blood or lymph stream metastasis must be admitted. I have seen cases of endometriosis in the abdominal wall; and one case of endometriosis in the lung, and one instance of endometriosis in an arm have been reported. I think lesions of this type, which are microscopically similar to endometrium, could only reach such sites by way of the blood or lymph stream.

Doctor Sampson's theory seems reasonable and possible, especially in these multiple, small lesions which are scattered through the pelvis. I think it accounts for many of the ovarian implantations. It seems possible that the ovary is very susceptible, especially in an area where there is recent corpus luteum, and that an endometrial cell, becoming implanted there, will grow rapidly and produce tarry cysts. The tarry cyst ruptures and spreads endometrial tissue throughout the pelvis. Cullen's theory of direct extension is also possible in many cases.

I believe many smaller areas never grow, and probably are destroyed or absorbed by the peritoneum.

Doctor Meigs referred to underdevelopment. I have not paid attention to the etiologic factor he mentioned, as much as I should, but in cases of congenital anomalies of the pelvic organs, including absence of the uterus, with normal ovaries and normal internal secretion, I have not seen a case of endometriosis, in spite of the fact that some of these patients have been married several years.

Doctor Meigs has covered the diagnosis and symptoms, and there is no doubt that "endometriosis-minded" surgeons make a preoperative diagnosis in a large number of cases, and, at operation, suspected tissues are removed and examined more routinely by competent pathologists.

None of us, including Doctor Meigs, recognized many cases 20 years ago, but Doctor Sampson, in Albany, was finding endometriosis in more than 20 per cent of the cases in which he performed abdominal or pelvic operations as long ago as that. As Doctor Meigs suggested, it is possible he was seeing selected cases, but the incidence of endometriosis in his cases seems large compared to the incidence in most of our cases. Many of us, I am sure, do not remove or record many pin-head-size areas of discolored peritoneum when operating for some other major pathologic condition.

Among younger women, when it seems advisable to perform conservative operations, I believe it is advisable to cut the presacral nerve at the time of pelvic surgery, in order to relieve dysmenorrhea, which is often a major complaint.

No group of benign gynecologic conditions causes me more concern than advanced and extensive endometriosis among young women. In recent years, I have been more conservative than formerly, especially with the use of roentgen or radium irradiation. Now, I believe, the patient's best interests are being served by saving some ovarian tissue, in spite of the risk that a second operation may have to be performed or menopausal dose of radium or roentgen irradiation administered at a later date.

DR. JOE VINCENT MEIGS (Boston, Mass., closing): I would like to add just one or two things. Not all cysts with chocolate fluid in them are endometriomata. The diagnosis must be made histologically before it can be accepted, and a great many of these cysts are not true endometriomata.

If children are born when a patient is young, and there is, thereafter, a long uninterrupted series of periods, fibroids are likely to occur as well as other benign pelvic growths. I do not think there is any question about it.

The percentage of endometriosis will increase in relation to the number of small suspected areas that are removed before the surgery begins, and put in solution for the pathologist to examine.

The most important deduction from the paper is that, if 36 per cent of 400 patients have endometriosis, it must indicate that endometriomata are not true tumors at all. They must represent abnormal physiology.



## INTRA-ABDOMINAL HERNIA—REVIEW OF 39 CASES IN WHICH TREATMENT WAS SURGICAL

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THE INCIDENCE of intra-abdominal hernia, treated surgically, is extremely low, as is shown by the fact that from 1910 to 1939, inclusive, only 39 instances of such a condition have been encountered at the Mayo Clinic. The occurrence of this condition, although rare, is much greater than this figure would suggest, for the majority of intra-abdominal herniae exist without producing symptoms and are discovered only at postmortem examination. Inasmuch as an intra-abdominal hernia may be an asymptomatic complication which is found incidentally during an operation for some other condition or which may be found to be the causative factor of some type of intestinal obstruction or the exciting influence for vague abdominal distress, pain or tumor, a review of our cases seemed justifiable.

Herniae that protrude, not through defects in the walls of the abdomen, but into an abdominal pouch or opening of the peritoneum, may be considered to be "intra-abdominal" or "internal herniae." These may be primary, a direct result of some congenital defect; secondary or postoperative sequelae; or referable to trauma or inflammation not the result of an operation. Thus, they include: (1) Those which occur in normal pockets, such as the foramen of Winslow, paraduodenal, paracecal, and intersigmoidal fossae; (2) those occurring in exaggerations of normal mesenteric folds, such as those in the broad ligament; (3) those resulting from traumatic or operative bands or adhesions; (4) those resulting from chronic inflammation; and (5) those which occur in anatomic defects.

A classification of internal herniae is difficult, but for the benefit of organization and presentation we have divided our cases into four groups: (1) Postoperative, 19; (2) paraduodenal, eight; (3) malformations, eight; (4) miscellaneous, four. Each group will be subdivided and discussed in some detail.

*General Considerations.*—In general, of the 39 cases, 21 (54 per cent) have been considered to be secondary, and 18 (46 per cent) primary. In 20 instances the hernia developed secondarily, previous to performance of some surgical procedure.

The symptoms presented by the herniae were, for the most part, varying degrees of intestinal obstruction. In 29 cases (74 per cent) the hernia was considered to be producing symptoms, and in 10 cases (25 per cent) no symptoms were caused. In the 10 cases in this latter group the hernia was an incidental observation at the time of operation for some other condition. The symptoms, for the most part, were vague and not characteristic. A preoperative diagnosis seldom was made. Some degree of obstruction of the small intestine was present in 28 (71 per cent) of the cases. In 19 cases (48 per cent) the onset was marked with acute obstruction of the small intestine. When obstruction was not present, pain or the presence of a tumor was the factor which prompted surgical intervention. In every case reviewed, operation was performed.

*Postoperative Hernia.*—Intra-abdominal hernia, as a postoperative complication, may be immediate or delayed. As a result of several factors, potential internal herniae are likely to afflict patients following performance of a surgical procedure. Failure of the transverse mesocolon to remain attached to the stomach following posterior gastro-enterostomy may result in an aperture through which a loop of small intestine may slip into the lesser peritoneal sac and cause obstruction. Adhesive bands resulting from inflammation can form the opening through which the bowel may herniate. These occur more commonly following various pelvic operations and secondary to operations for ruptured appendix. Twenty such cases are included in our series.

Herniation of the small intestine through the transverse portion of the mesocolon into the lesser peritoneal cavity evidently was an occasional occurrence early in the history of gastro-enterostomy. Hernia of the small intestine through a congenital opening in the transverse part of the mesocolon has been reported, but is exceptionally rare. When this condition occurs it can be recognized easily at operation and presents little difficulty in treatment. When a hernia is found in the lesser peritoneal cavity and the foramen of Winslow is patent, an opening should be looked for in the transverse part of the mesocolon. Since surgeons, appreciating the risks involved, have been increasingly careful to close the edges of the openings in the transverse part of the mesocolon around the stomach and jejunum, herniation into the lesser peritoneal sac has become infrequent. Although the majority of internal herniae occurring secondarily to gastro-enterostomy have occurred because a portion of the small intestine slipped through the artificial opening in the transverse part of the mesocolon, a few other types of herniation have occurred. In these few, the intestine slipped behind the loop of jejunum which is formed by every anastomosis, whether it is antecolic or retrocolic. After performance of posterior gastro-enterostomy, the proximal loop of jejunum is attached at two points, namely, the duodenojejunal junction, and the stoma. This forms an artificial foramen bounded posteriorly by the peritoneum over the vertebral column, superiorly by the transverse part of the mesocolon and stomach, and anteriorly and inferiorly by the jejunum.

## INTRA-ABDOMINAL HERNIA

This foramen can be avoided by shortening the proximal loop employed in performing gastro-enterostomy and by suturing the margins of the opening together, utilizing the jejunum and transverse portion of the mesocolon. In spite of the fact that these various openings are closed at the time of operation, herniae have developed in a certain number of patients. This occurrence may be referable to some error in technic in the closure, or to inflammation, rapid absorption of the suture material used, or subsequent trauma.

There were ten cases in this series in which an internal hernia developed secondary to performance of gastro-enterostomy. In eight instances, posterior gastro-enterostomy, and in two, anterior gastro-enterostomy, had been performed. In six instances, the hernia occurred through the transverse part of the mesocolon. The bowel was herniated behind the proximal limb of jejunum in the retrocolic position in two instances, and in the remaining two, it was herniated behind the jejunum in its antecolic position. In two cases, the symptoms necessitated surgical treatment within one week after performance of gastro-enterostomy, whereas in the remaining eight cases a period of from three to eight years had elapsed from the time of performance of gastro-enterostomy to the secondary operation. In three instances, the symptoms were classed as "acute intestinal obstruction" and in seven cases, the symptoms were intermittent, vague, and of a chronic nature. Of the seven cases in which the patients were not operated upon for acute symptoms, a gastrojejunal ulcer had been suspected before the operation, but in only three instances was a gastrojejunal ulcer actually present. The hernia produced symptoms in nine cases; in three, acute intestinal obstruction, and in six, varying degrees of intestinal obstruction. The symptoms in the tenth case were attributed to gastrojejunal ulcer and the hernia was considered to be an incidental finding. Although roentgenographic examinations were made in every instance, and although the possibility of a mechanical defect was suspected, the preoperative diagnosis of herniation was not made in any case.

It is probable that in some cases intra-abdominal hernia develops following performance of gastro-enterostomy for peptic ulcer but the hernia goes unrecognized. Other herniae have been reported to afflict patients following resection of the stomach with anastomosis to the jejunum. The presence of this type of hernia is difficult to recognize, but in those cases in which gastrojejunostomy has been performed and symptoms of intestinal obstruction develop, or in which some mechanical defect in the anastomosis is present, the possibility of herniation must be considered. Such herniae can be prevented for the most part by accurate closure of all openings in the transverse part of the mesocolon and by obliteration of the gastrojejunal hiatus. The following case is typical:

**Case 1.**—A woman, age 24, had undergone posterior gastro-enterostomy in 1936 for duodenal ulcer. Six months after the operation, distress developed which was different

from that which had been present prior to operation. About one hour after the eating of a heavy meal, she became "bloated," experienced mild cramp-like sensations in the midepigastrium, and a sense of pressure beneath the xiphoid process. One evening she was awakened by severe, intermittent colicky pain in the epigastrium; this was associated with persistent nausea and frequent vomiting of bile-tinged vomitus. The pain gradually localized in the left side of the abdomen, and operation for acute intestinal obstruction was advised. At operation, the entire small bowel was found to be obstructed and protruding through a small opening in the transverse portion of the mesocolon just adjacent to the site of anastomosis. This hernia was reduced and the opening was closed. The patient has remained free of symptoms since.

Occasionally, the intestinal obstruction has occurred secondarily to an intra-abdominal hernia caused by the formation of an aperture lateral to the loop of colon brought out during colostomy. Two such cases are included in our series. A typical case has been reported by C. H. Mayo and Magoun.<sup>5</sup>

Although the previously mentioned type of hernia occurs infrequently, every precaution should be taken to avoid it. This can be done by carefully and securely closing with sutures the mesosigmoid to the left parietal peritoneum. The finger should be inserted to demonstrate that all openings which might be potential causes of hernia have been closed.

Following an operation for retroversion, some error in technic may occasionally be the cause of formation of a potential internal hernia. This type of hernia has occurred most frequently following performance of the Baldy-Webster type of operation, during which the suturing of the broad ligament to the round ligament at the points of perforation of the broad ligaments was either overlooked, or after which the suturing has secondarily broken down. On the other hand, the round ligaments may be drawn through the broad ligaments too far away from the body of the uterus, so that, secondarily, a strain on these ligaments may cause the round ligaments to cut through the broad ligaments toward the median line, thus producing an aperture through which herniation of small intestine may occur.

Occasionally, in patients for whom no previous surgical treatment has been instituted, pouches and openings in the broad ligaments have been observed. These, for the most part, are considered to be congenital in origin, but in certain cases it is possible that distention and stretching arising from pregnancy, from a large pelvic tumor, or from a pelvic inflammatory disease may have produced them.

In other instances, in performing such operations as myomectomy, oophorectomy, appendicectomy, and the like, openings are inadvertently made in the broad ligaments. These may go unobserved and become potential causes of herniae. In the performance of other pelvic operations in which the uterus is suspended, instances of herniation of intestine between the uterus and anterior abdominal wall have been reported.

Three patients in our series had hernia of the broad ligaments. In two cases these herniae followed performance of the Baldy-Webster type of operation for retroversion. In each of these cases, an acute intestinal obstruction was present, whereas in the case in which the hernia was of con-

genital origin, the tube and ovary had herniated themselves into a pouch in the right broad ligament and were producing symptoms. The following case is typical:

**Case 2.**—A woman, age 47, had undergone a Baldy-Webster type of operation 16 years before admission to the Mayo Clinic. Thirteen years before her admission to the Clinic she had an internal shortening operation. On her admission a diagnosis of obstruction of the small intestine was made. At operation, two loops of strangulated ileum were found to have herniated through the right broad ligament. The hernial opening was situated just below the utero-ovarian ligament, where the round ligament had been pulled through a perforation in the broad ligament.

Herniation of this type can be prevented if all points of perforation in the broad ligaments are closed at the time of operation. In performing such operations as ventral fixation, Gillian suspension and the like, the surgeon should be careful to leave no aperture through which herniation may occur. This condition can be suspected when the symptoms of acute intestinal obstruction occur in a patient following performance of operative suspension for fixation of the uterus.

In five patients in our series, acute intestinal obstruction developed subsequent to the formation of intra-abdominal hernia as a result of previous surgical treatment. In each of these cases, there was a history of infection or peritonitis following the previous operation. Herniae of this type may develop during immediate postoperative convalescence, but as a rule are discovered a number of months or even years later, when the patient is admitted for an acute intestinal obstruction. In the five cases, the obstruction developed 4 and 6 weeks, and 8, 14, and 16 years following performance of the original operation. In three instances, the herniae were secondary to operations for ruptured appendices, and in the other two instances, pelvic operations had been performed:

**Case 3.**—A woman, age 43, had undergone a suspension operation for fixation of the uterus and also appendicectomy in 1924, and, in 1936, abdominal hysterectomy had been performed. One month following this operation, acute obstruction of the small intestine developed. At operation, a gangrenous loop of ileum was found to have herniated behind a firm fibrous band which extended from the left pelvic wall to the region of the stump of vagina. The gangrenous portion of bowel was resected, and side-to-side ileo-ileostomy was performed.

Adherent loops of intestine may form unusual apertures:

**Case 4.**—A woman, age 30, had undergone appendicectomy for a ruptured appendix in 1922. In 1938, an acute obstruction of the small intestine suddenly developed. At operation, a loop of small intestine was found to be adherent to the terminal portion of the ileum. One end of the loop was attached to the mesenteric border and the other to the mesenteric border. Through this loop 6 cm. of ileum had herniated, causing obstruction.

Various apertures may occur in the omentum as a result of trauma or infection:



**Case 5.**—A man, age 55, had undergone an operation for drainage of an appendiceal abscess in 1930, and later in the same year had undergone appendectomy. He was admitted to the clinic with an acute intestinal obstruction. At operation, a strangulated loop of ileum was found to have herniated through some adherent omentum in the right side of the lower portion of the abdomen. The edges of this aperture were thickened and fibrous. The obstruction was relieved by division and resection of this portion of omentum.

*Paraduodenal Hernia.*—The literature pertaining to paraduodenal hernia is voluminous.<sup>1, 3, 6, 9, 10, 11, 12</sup> An exuberant and diversified nomenclature has accumulated, with chaotic results, and the underlying facts seem to have been lost to complete analysis. Many fossae about the duodenum have been minutely described, but proof that they are a factor in the causation of such herniae is lacking.

Left duodenal herniae occur much more frequently than do those on the contralateral side. Bryan,<sup>2</sup> in 1935, stated that 162 of the former and only 43 of right duodenal herniae had been reported. Many of these herniae are never recognized during life and are found either at the postmortem table or accidentally when the abdomen is explored for other reasons. Such a state of affairs will be considered logical when it is realized that the herniae, as such, do not produce symptoms. It is only when obstruction, acute or chronic, or strangulation supervenes, that patients present themselves for treatment.

Diagnosis of a duodenal hernia is a rare feat. Of 91 cases of left duodenal herniae which Pikin<sup>7</sup> collected, in only three was the condition diagnosed clinically. After careful analysis of his collected cases, Moynihan<sup>6</sup> was able to offer some excellent suggestions which would permit a diagnosis to be made. In addition to the signs of acute intestinal obstruction, he noted that (1) a localized swelling of the abdomen will be present, the position of the tumor resulting from the side affected, and that around such a mass is a region of compression corresponding to the position of the colon; (2) the tumor may be distinctly delineated by palpation, and although sounding flat to superficial percussion, it will be rather resonant to deep percussion; (3) gurgling sounds may be heard anywhere in the tumor; and (4) in left duodenal herniae, because of the position of the inferior mesenteric vein in the neck of the sac, symptoms of venous obstruction may be evident. Blood may be found in the stool, hemorrhoids may be present, or dilated veins may be present on the anterior abdominal wall.

Eight "duodenal herniae" were encountered in the present series, and of these, six were on the left and two were on the right. Seven of the patients were men. The ages of these patients were between 32 and 59. In association with that which has been written previous to the production of symptoms, it is interesting to note that only two of these patients gave a history of abdominal pain and discomfort. It is likewise important to note that in one the duration of symptoms was 20 years and in the second, four years. Five of the herniae were discovered at operation for other pathologic conditions

of the upper part of the abdominal cavity, whereas exploration in the remaining three patients was undertaken because of unexplained abdominal symptoms. Masson and McIndoe<sup>4</sup> have reported on one of the latter previously. Their patient had a large, right duodenal hernia, but the obstructive symptoms present were the result of a localized portion of hyperplastic tuberculosis in the ileum.

**Case 6.**—A male, white, age 40, stated that he had had recurrent attacks of left abdominal pain for approximately four years. During the two years just prior to his registration, symptoms referable to intestinal obstruction were present. Tarry stools have been noted occasionally. During this period of four years, the patient had lost about 25 pounds (11 Kg.).

Physical examination disclosed nothing abnormal save for abdominal tenderness over the region of the left portion of the colon. The patient had the sensation that an indefinite abdominal mass was present. Results of roentgenographic studies of the stomach and large bowel were normal; and a study for intestinal stasis revealed that the barium was distributed throughout the bowel in 16 hours. It was suggested that some unexplained type of pathologic process was present and that the latter might be either a diaphragmatic hernia or some other type of internal hernia. Surgical exploration was advised.

At operation a definite hernial opening was found at the duodenojejunal junction just under the ligament of Treitz. The opening to the hernial sac was closed. It is likewise interesting that a Meckel's diverticulum was also found in this patient.

*Herniae Referable to Congenital Malformations.*—Instances of congenital malformation of the primary midgut loop, excluding the duodenal hernia, also form an interesting group. Such abnormalities have their origin in malrotations or improper fusion of the peritoneal layers, either of the mesentery of the small intestine, or of the cecum and ascending part of the colon. Persistent traction bands may also be found in such cases. Defective disposition of the small intestines and right part of the colon, a process commonly termed "malrotation," accounted for the production of hernia in two individuals. A report of one of the cases follows:

**Case 7.**—The second of these patients was a boy, age three, who had been subject, since birth, to frequent episodes of vomiting, which had been marked during the first 18 months of life but which, during the year prior to the patient's registration, had occurred but once every two to four months. During these attacks the child would double up as if abdominal pain and cramps were present. Diarrhea or constipation was not noted.

The abdomen was moderately distended and an intestinal pattern was seen. However, peristalsis was not audible. Because of the persistence of regurgitation and the onset of other signs of partial high intestinal obstruction, the abdominal cavity was explored. The stomach, duodenum, and upper portion of the jejunum were distended, but the small bowel distally was collapsed. A persistent traction band, situated about eight inches (20 cm.) from the ligament of Treitz, had almost completely occluded the jejunum. Associated with this anomaly was a clockwise malrotation of 90° of the postarterial segment of the primary midgut loop to the right. This malrotation had caused the cecum and ascending part of the colon to occupy their usual positions. However, the small bowel lay almost completely on the left side of the abdomen. The transverse part of the colon was anterior to the superior mesenteric vessels, whereas the jejunum lay

posterior to the trunks. Symptoms probably were almost completely referable to the persistent traction band.

Improper fusion of the peritoneal layers of the postarterial segment will result in the formation of small pouches under the cecum and ascending part of the colon. Retrocecal hernia were found incident to performance of surgical procedures for other conditions in two patients. Neither had had symptoms. Reduction of the hernial mass, which may be composed of portions of the ileum, or ileum and cecum, is followed by simple suture of the orifice.

**Case 8.**—A second variety of paracecal hernia was found in a male, age 25, who complained only of moderately severe abdominal pain. A region of extreme tenderness was present in the epigastrium. Results of roentgenographic examination of the stomach were normal, but studies of the colon revealed that a transposition was present. Upon exploration, a herniation of practically all the small intestine through an opening just beneath the ileocecal valve was found. The aperture was large enough to admit three fingers. An extremely mobile cecum was present. Reduction of the hernia was accomplished by incision of the outer leaf of the peritoneum of the mesentery of the right part of the colon.

In similar manner, prolapse of the ileum into a sac under the mesentery of the small intestine may also occur.

**Case 9.**—A male, age 34, had suffered recurrent attacks of pain in the right lower abdominal quadrant. Acute appendicitis was the preoperative diagnosis, but exploration revealed an obliterated appendix. Additional search demonstrated that a hernia involved 12 inches (30 cm.) of ileum. Additional interest in this case was provided by the presence of a Meckel's diverticulum.

An internal hernia, involving the mesentery of the small intestine, but in a somewhat different situation than that just presented, may be found when prolapse of the bowel through an aperture lying between the ileocolic artery and its last mesenteric branch has taken place. Such apertures may be either congenital or they may result from thinning of the mesentery caused by one of several factors. The passage of a loop of intestine through such a hiatus is one of the more uncommon mechanisms producing acute intestinal obstruction.

The occurrence of internal herniation through the foramen of Winslow is extremely infrequent, because of the barrier afforded by the transverse part of the colon. In addition, the anterior and the posterior boundaries of the aperture are, as a rule, in direct contact. According to Moynihan, one of the following factors must be present to permit the formation of this particular type of hernia: (1) A common mesentery for the whole intestine; (2) absence of secondary fusion of the ascending part of the colon to the abdominal wall; (3) an abnormally large foramen, and (4) an abnormal length of the mesentery and consequent marked mobility of the intestine. Pain experienced by such patients is usually epigastric and a tumor can usually be felt in the same situation. A resonant note is obtained on deep

percussion over the mass. The usual signs of acute intestinal obstruction are present.

**Case 10.**—Illustrative of herniation through the foramen of Winslow is the condition of a woman, age 56, who had suffered epigastric pain for three and one-half days. Nausea and vomiting were marked. On admission, considerable distention of the abdomen was evident and borborygmi could not be heard. Because of her poor physical condition, simple enterostomy alone was performed. The patient improved to such an extent during the succeeding 24 hours that further operation seemed indicated. The cecum and the ascending part of the colon were found to have prolapsed through the foramen of Winslow into the lesser peritoneal cavity. A condition which might be termed "hernia of a hernia" was also present, for part of the bowel had ruptured through the anterior leaf of the lesser omentum and was hanging down anterior to the stomach. This loop was distended and discolored. Decompression of the affected bowel was effected and the hernia was reduced. A catheter was sutured into the bowel at the point at which the gas had been withdrawn.

*Miscellaneous Considerations.*—A few cases could not be satisfactorily classified in any of the above mentioned groups, so we have placed them in a miscellaneous group. There were four such instances, one of which already has been discussed in the section of this paper concerned with postoperative herniae into the broad ligaments.

Occasionally, secondarily to some inflammatory condition such as pelvic inflammatory disease, appendicitis, and the like, for which no surgical intervention has been undertaken, adhesive bands may form. In some instances, a Meckel's diverticulum may remain attached to the abdominal wall, producing a band-like structure. These bands and adhesions are occasionally the cause of herniation, with resulting intestinal obstruction.

It is difficult to explain the causation of mesenteric and omental defects and, in the absence of a suggestive cause, many are thought to be congenital. Rupture of either of these defects as a result of external violence and injury during the course of a previous operation are considered to be possible causes. In some cases, antecedent inflammation of the appendix with involvement and subsequent atrophy of mesentery or omentum may produce such a defect.

Stalker and Gray<sup>8</sup> have previously reported a case of herniation into the prevesical space, or the space of Retzius. This was the sixth prevesical hernia to be reported in the literature. Several theories have been presented as to the origin of this type of hernia but in the absence of both trauma and a previous operation we feel that it must be considered to be secondary to some congenital defect.

*Comment.*—Were it not for the fact that internal herniae become manifest through various degrees of intestinal obstruction, the majority of such herniae would pass without recognition. Occasionally, in performing an operation for some unrelated condition, an anomalous condition is found which may prove so confusing that it may seriously complicate the necessary surgical procedure. Inasmuch as these conditions may exist without producing symptoms, the surgeon should not attempt surgical repair in every case. As we

have pointed out, the majority of so-called paraduodenal herniae are not associated with symptoms. This is also true of certain of the herniae associated with malrotation of the colon. Extensive surgical intervention would be required to repair these congenital defects satisfactorily, and in many instances a satisfactory repair of the defect could not be accomplished. Thus, it is our conclusion that all general surgeons should be familiar with the anatomic aspects of various types of intra-abdominal herniae, but that for the most part they should be conservative in their treatment when such herniae are found incidentally and are not producing serious symptoms. On the other hand, the presence of such herniae must be suspected in all cases of intestinal obstruction, either partial or complete. Treatment in these circumstances will be essential and will vary with the anatomic circumstances present at operation. Because such herniae frequently are associated with bizarre and not characteristic symptoms, their presence and the early recognition of the resulting obstruction of the small intestine may be overlooked. Because a preoperative diagnosis is seldom made, the problem of the correct treatment in the individual case may be difficult, and must be decided upon while the patient is on the operating table. In many of these cases, strangulation is present and immediate surgical treatment must be instituted. It has been our experience that the various adjuncts in the treatment of intestinal obstruction, namely, an indwelling intestinal catheter, administration of 95 per cent oxygen, and other conservative methods of intestinal decompression, have frequently been employed for undue periods for those patients who should have been operated upon immediately. Too great emphasis cannot be placed on the necessity of distinguishing accurately those conditions which are not amenable to such conservative treatment. It may be (and in this small group of cases of intra-abdominal hernia will be) impossible to make such a decision and, if doubt exists, fewer mistakes will be made by performing surgical exploration.

## SUMMARY

Thirty-nine cases of intra-abdominal hernia, in which the patients were treated surgically at the Mayo Clinic between 1910 and 1939, inclusive, have been reviewed.

Eighteen herniae were considered to be primary, or directly the result of some congenital defect.

Twenty-one herniae occurred secondarily to operation, trauma, or inflammation. Symptoms were manifested by the herniae in 29 cases, and in ten cases the herniae were found incidental to operation for another condition. Some degree of intestinal obstruction was present in 28 cases, and in 19, acute intestinal obstruction developed. The histories of several patients illustrating the various types of intra-abdominal herniae found, have been presented.



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## TESTICULAR TRANSPLANTATION

### SUCCESSFUL AUTOPLASTIC GRAFT FOLLOWING ACCIDENTAL CASTRATION

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LOSS OF THE TESTICLES in the adult as the outcome of criminal or punitive castration, traumatic accident and self-inflicted removal results in serious metabolic disturbances involving not only sexual functions but especially the nervous and muscular systems. Early recovery of the testicles with reimplantation into the scrotal region, observing certain physiologic considerations, offers the possibility of successful grafts. This procedure naturally is not applicable when surgical castration is performed for the removal of diseased testicles.

When the implanted tissue originates in the host it is called autogenous. The operation is termed autoplasmic transplantation or reimplantation. The transplanted tissue becomes a graft after evidence is present that it "takes" or survives.

In transplants, the survival of viable testicular cells is dependent upon nutrition resulting from the penetration of a compatible host's circulation into the transplanted tissue which consequently must be inserted in such form as to expose a large proportion of incoming cells to vascularization by the host. Reimplantation of the whole testis, or large portions of it, into any part of the body has invariably resulted in little benefit and later sloughing. Tissue in the form of thin slices or mush injections are most apt to result in successful grafts.

Carl Moore's experiments have produced convincing proof that the testis attains its full development and functional capacity in the scrotum where the temperature is from three to six degrees below that of the internal parts of the body. A local tissue peculiarity in the scrotum may also be a factor in normal testicular development. The choice of the scrotum as the site for implantation is the *most important prerequisite* for success. The dartos layer is an ideal location for the introduction of transplants because of the total absence of fat, the presence of loose areolar tissue, the proper temperature and good vascularity.

The record of a patient observed over a period of two and one-half years is appended:

**Case Report.**—On October 12, 1937, a hospital call from Dr. H. G. Oakland brought the author to the pathetic sight of a young man, age 23, whose right arm had been amputated just below the elbow; and both testicles, scrotum and the skin of the penis had been torn from his body. The accident had occurred less than one hour previously. While working in a box factory he had leaned forward over a lathe carrying a revolving knife

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FIG. 1.—External genitals as they appeared after recovery from underwear.



FIG. 2.—Appearance of the genitals before preparation for operation. The penis is denuded except for the semimucosal or inner part of the prepuce.

when his trousers were caught up and quickly wound into the machine. His right hand grasped his trousers, was drawn into the whirling knife and amputated together with the external genitals. On arrival at the hospital he was in shock—severely exsanguinated. Doctor Oakland had controlled the bleeding in the arm stump. There was no bleeding from the genital wounds. With the aid of three blood transfusions during the night there was rapid recuperation.

The scrotal skin, intact testicles and the skin of the penis, still attached to one another, were found in the patient's underwear and placed in a refrigerator overnight in a normal saline dressing (Fig. 1).



FIG. 3.—Photograph showing complete healing, with little distortion and full erectile function.

The following morning, under general anesthesia, working concurrently with Doctor Oakland who repaired the arm stump, reconstruction of the genitals was carried out. Fourteen sliced cross-sections of testes, each about 2 Mm. in thickness, were implanted in the scrotal wound and covered with the flaps of the remaining scrotal skin. One section of epididymis was also implanted.

The accident left the semimucosal or inner part of the prepuce still covering the glans (Fig. 2). This part of the prepuce was simply inverted over the glans and covered about 3 cm. of the distal part of the shaft, where it was held in place with a few interrupted catgut sutures. The remainder of the denuded penis was covered with a full-thickness graft made up of a collar of the very skin which had been torn from this area. All of the skin grafting was successful except the full-thickness one on the proximal part of the shaft which survived in only isolated areas and had to be largely replaced at several later sittings with pinch-grafts taken from the thigh. The patient left the hospital, December 14, 1937, apparently well, with a normally functioning penis (Fig. 3).

Naturally, the pertinent questions concerning this patient are: (1) Have the testicular transplants been successful; and (2) how long will the grafts function? For an answer to these questions one must consider the prostate gland which is the most sensitive clinical indicator of testicular function. Experimentally, in castrated male animals, the administration of androgenic agents is promptly followed by an increase in size of the atrophied prostate

# TESTICULAR TRANSPLANTATION

and seminal vesicles. This reaction, in fact, is the basis of an assay method. Carl Moore, Deansly, McCullagh and others have called attention to the prompt atrophy of the prostate following castration.

*Subsequent Course.*—True to form, our patient at the end of two and one-half weeks had developed a very definite shrinkage in the size of the gland. Instead of the usual succulent gland, typical of young men at his age, it had shrunk at this early post-operative stage to about one-half normal size. At the end of six weeks it was barely palpable and at three months could be outlined with difficulty by rectal palpation. Continued periodical rectal examinations revealed a gradual regeneration of prostatic tissue during ensuing months, indicating that the grafted testicular cells were surviving and probably elaborating secretion (Chart 1).

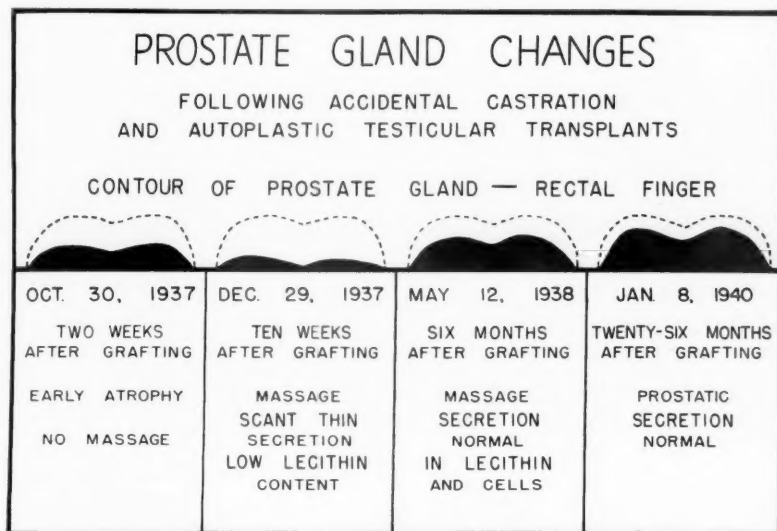


CHART 1.

He has remained normal since that time, regained his full vigor and endurance, has normal libido and frequent erections, and has experienced ejaculations about once monthly. A number of definite nodules in the scrotal region at the site of the grafts, some the size of a pea, have persisted.

There has been no deviation from normal in numerous repetitions of the following tests: Friedman test for gonadotropin, basal metabolism test, blood cholesterol and sugar tolerance. Tests for the presence of androgenic hormones in the urine demonstrated increasing excretion of androgens. The last assay, completed August 19, 1939, showed an output of approximately 57 international capon units per day as compared to an output of 20 to 30 capon units per day during the first weeks following the operation (Chart 2). Because of the normal clinical course there has been no administration of either the extracts of thyroid, anterior pituitary-like substance or of testicular hormone at any time during his convalescence.

**COMMENT.**—The result in this patient has been very gratifying up to the present and we are hopeful that prolonged function will be realized. The grafted tissue in this patient possesses two essential qualifications for success: First, it is autogenous, being returned to its original host; and, second, it has been placed in its normal scrotal habitat. The early atrophy and then



regrowth of the prostate gland indicates that there was, primarily, a lack of cellular function but, later, adaptation and regeneration took place. The increasing urinary excretion of androgens now adds to the encouraging outlook.

The precautions required in tissue culture and transplantation were observed, namely: The reimplantation was carried out as promptly as possible after removal; sudden and repeated changes in temperature were avoided as well as direct exposure to sunlight; and there was no undue trauma or drying.

The successful result in this patient prompted an attempt to graft testicular tissue into human castrates. Homoplastic transplantation was recently performed on two castrates, who received injections under the scrotal skin

RECORD OF TESTS ON GRAFTED CASTRATE J.A.							
DATE	BLOOD HEMOGLOB	FRIEDMAN GONADOTROPHIN TEST	BASAL METABOLISM	URINARY ANDROGENIC ASSAYS	BLOOD CHOLESTEROL	GLUCOSE TOLERANCE TEST	
NOV. 6 1937	58%	NEGATIVE	+93%	22 CAPON UNITS DAILY FIVE DAY COLLECTION	119.8 MGS.	BLOOD SUGAR BEFORE 108.8 1/2 HOUR AFTER 184.3 1 HOUR AFTER 174 2 HOURS AFTER 150.4 3 HOURS AFTER 87.3	ONE HOUR URINE POS. WITH 5 GTTS. TWO HOUR URINE POS. WITH 10 GTTS. OTHERS NEGATIVE
DEC. 15 1937	78%	NEGATIVE	+81%	27 CAPON UNITS DAILY FIVE DAY COLLECTION	159.2 MGS.	BLOOD SUGAR BEFORE 99 1/2 HOUR AFTER 188.9 1 HOUR AFTER 187.4 2 HOURS AFTER 98.5 3 HOURS AFTER 93	ALL URINE SUGAR NEGATIVE
APR. 27 1938	80%	NEGATIVE	-17.5%	44 CAPON UNITS DAILY FIVE DAY COLLECTION	127.9 MGS.	BLOOD SUGAR BEFORE 101 1/2 HOUR AFTER 120.5 1 HOUR AFTER 113.6 2 HOURS AFTER 87.3 3 HOURS AFTER 79.2	ALL URINE SUGAR NEGATIVE
JAN. 8 1940	94%	NEGATIVE	-4%	57 CAPON UNITS DAILY FIVE DAY COLLECTION	183.1 MGS.	BLOOD SUGAR BEFORE 102.6 1/2 HOUR AFTER 125.8 1 HOUR AFTER 149.3 2 HOURS AFTER 105.5	ALL URINE SUGAR NEGATIVE

CHART 2.

of a testicular mush made up of the testicles of a young man killed in an accident. Preliminary blood grouping of donor and recipients was carried out. Their compatibility was established. This most important step is usually overlooked. A report on the results of these operations and others to follow will be published after several years of observation.

## SUMMARY

(1) Autoplastic testicular transplants were carried out in a patient, age 23, following accidental castration.

(2) Successful graft resulted. Observation during two and one-half years demonstrated regeneration of the prostate gland, normal sexual behavior, and the persistence of normal clinical and laboratory tests.

(3) The method of transplantation herein described is recommended for the replacement of testicular tissue which is lost in the maneuvers of warfare.

## THE PRESENT STATUS OF INTRAVENOUS FLUID TREATMENT OF TRAUMATIC AND SURGICAL SHOCK\*

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INTRAVENOUS fluid replacement therapy is one of the chief elements of modern shock treatment. The need for such replacement is evident because of the importance of oligemia in shock. This factor is of such importance that in the recently published British M. R. C. Memorandum, No. 1,<sup>71</sup> "The Treatment of Wound Shock," the following statement was made: "It is now generally accepted that the most important requirement for arresting the progressive deterioration in general condition which is such a feature of shock, is restoration of blood-volume and thereby of tissue metabolism." In a recent definition of shock—progressive vasoconstrictive oligemic anoxia—one of us (H. N. H.) further emphasized the importance of the *oligemia* and inferred the need for prompt treatment before the *progressive* state had irreversibly injured the body by means of the *anoxia*.

Since the ideal method of correcting the oligemia would be to replace fluid exactly similar to that lost, this should be the ideal toward which therapy should be directed. It is difficult, however, in many cases to be sure just what blood elements have been lost and, even if known, such fluids are not always available. In some cases of shock, the fluid lost is essentially whole blood, in other instances, it is practically pure plasma. Various clinical cases run the entire gamut of possibilities between these two extremes. In other cases, more than one separate injury may be present—as, for example, a burn complicated by abdominal trauma and bleeding into the peritoneal cavity.

In the present paper, the various fluids that can be used intravenously in the treatment of shock are reviewed and the indications and contraindications for each are discussed. A few experimental observations on the fate of certain of the various fluids are cited. The fluids used may be listed as shown in Table I.

### (I) SALINE CRYSTALLOID SOLUTIONS

These solutions have the advantage of ready availability, almost permanent preservability, and absence of toxicity, but recently a collection of evidence has been built up to show that in shocked patients their stay inside the blood vessels is only temporary. Furthermore, the more advanced the shock and the more imperative the need for treatment, the less apt are crystalloid solutions to be of benefit. Pilcher and Sollmann<sup>82</sup> (1914); Krogh<sup>63</sup> (1922);

\* Presented by title before the American Surgical Association, White Sulphur Springs, W. Va., April 28, 29, 30, 1941. To Doctor Harkins goes all credit for the work on this paper.—Roy D. McClure.

TABLE I

PARTIAL LIST OF BLOOD SUBSTITUTES USED IN INTRAVENOUS REPLACEMENT  
THERAPY OF SHOCK

- (1) Saline crystalloids (normal salt solution, Ringer's solution, Locke's solution, *etc.*)
- (2) Glucose solution
- (3) Gum acacia solution
- (4) Gelatin-saline solution
- (5) Amino-acid solution
- (6) Casein digestate
- (7) Ascitic fluid
- (8) Whole blood
  - (a) Direct transfusion
  - (b) Citrated fresh blood
  - (c) Citrated preserved blood
  - (d) Placental blood
  - (e) Cadaver blood
- (9) Plasma
  - (a) Natural plasma
  - (b) Reconstituted normal plasma
  - (c) Reconstituted concentrated plasma
  - (d) Calcificated plasma
  - (e) Heterologous (bovine) plasma
- (10) Serum
- (11) Red cell solution
- (12) Hemoglobin-Ringer solution

Kinsman, Spurling, and Jelsma<sup>61</sup> (1928); Miller and Poindexter<sup>72</sup> (1932); Roberts and Crandall<sup>84</sup> (1933); Adolph, Gerbasi, and Lepore<sup>1</sup> (1934); Horsley<sup>55</sup> (1934); Amberson<sup>3</sup> (1937); Hepler and Simonds<sup>49</sup> (1938), and Wakeley<sup>93</sup> (1940) noted the ease of escape of these solutions from injured blood vessels. Whitby<sup>95</sup> (1941) stated: "The effect of saline is evanescent." Best and Taylor<sup>11</sup> (1939) also recognized the short stay of crystalloid solutions in certain surgical cases, stating: "If the blood volume has been reduced as a result of hemorrhage or shock, the intravenous injection of a saline solution, owing to the short stay of this fluid in the blood stream, is of little value, and may indeed be harmful. Transudation of fluid into the tissue of the lung—pulmonary edema—may result."

Hill, McMichael, and Sharpey-Shafer<sup>50</sup> (1940) also made observations on the transiency of action of crystalloid solutions. They found that "physiologic or hypertonic saline given intravenously to normal people is rapidly lost from the circulation" and that "in shocked patients intravenous saline produces transient benefit only." Similar observations were made by Maes and Davis<sup>70</sup> (1941), stating: "When the reduction in blood volume has existed long enough to produce, through oxygen lack, increased permeability of the capillary walls, administration of such solutions may result in a further loss of plasma proteins from the blood stream." These authors pointed out that advocacy of crystalloid solutions in shock treatment by MacFee and Baldridge<sup>67</sup> (1930) and by Hoitink<sup>53</sup> (1935) may depend on a consideration of cases seen before marked increase in capillary permeability has occurred.

Davis<sup>33, 34</sup> (1937) performed experiments which indicated that excess use of crystalloid solutions may be harmful in shock. A diminution in oxygen usage occurred in such cases which Davis termed an "anoxemic response."

The most complete exposition of this aspect of the subject, however, was

made by Blalock, Beard,<sup>8, 9, 10, 13, 14, 15</sup> and their associates (1932 and 1933) in a series of six experimental papers. They found that saline or glucose injections would actually wash plasma proteins out of the blood stream, causing the animals to be poorer in plasma protein than they would have been if not treated at all. Further extensive studies of Minot<sup>73</sup> (1937), and of Minot and Dodd<sup>74, 75</sup> (1940 and 1941), have corroborated these observations. Minot and Dodd<sup>74</sup> (1940) stated: "When plasma protein is deficient, the administration of fluid alone fails as a means of restoring an adequate volume of blood. Indeed, such measures often result in a greater loss of protein through injured capillaries."

Buttle, Kekwick, and Schweitzer<sup>24</sup> (1940) performed a series of experiments shown in Table II. These experiments indicated that isotonic saline easily passes from the circulation into the tissues and is unable to raise the blood volume for more than a brief time. Cats were bled 50 per cent of their calculated blood volume as rapidly as was compatible with life, and then the blood volume was restored with various blood substitutes. It is seen that not only all of the untreated controls, but all the saline injected animals died. It is also seen that of the 12 blood substitutes tested, only three (plasma, dried plasma of Greaves, and filtered plasma) were as efficacious as whole blood in restoring the blood pressure of cats in shock to normal. It is also seen from the table that only seven of the 12 saved the lives of all the cats tested. Buttle and his associates rated the blood substitutes in the following order of merit: Plasma, serum, hemoglobin-Ringer, gum acacia, red cell solution, isotonic saline; and last, isotonic glucose.

TABLE II

EXPERIMENTS OF BUTTLE, KEKWICK, AND SCHWEITZER (LANCET, 2:507, 1940) ON RELATIVE MERITS OF DIFFERENT BLOOD SUBSTITUTES IN RESTORING BLOOD PRESSURE OF CATS RAPIDLY BLED 50 PER CENT OF THEIR BLOOD VOLUME

Fluid Replaced	No. of Expts.	Deaths	Av. Vol. of Fluid Given (cc.)	Blood Pressure Response
(1) None.....	7	7	None	None
(2) Whole blood.....	5	0	83	Good and maintained
(3) Normal salt.....	5	5	95	Poor and transient
(4) Normal glucose.....	5	5	89	Poor and transient
(5) Acacia.....	8	3	93	Fair with slight later fall
(6) Hemoglobin-Ringer.....	5	0	75	Good with slight later fall
(7) Cells.....	6	3	75	Fair but temporary
(8) Plasma.....	7	0	70	Good and maintained
(9) Serum.....	7	0	72	Good with slight later fall
(10) Dried serum.....	3	0	66	Fair and maintained
(11) Dried plasma (Davie).....	6	6	25	All died at end of injection
(12) Dried plasma (Greaves).....	3	0	79	Good and maintained
(13) Filtered plasma.....	5	0	81	Good and maintained
(14) Plasma-saline.....	3	0	69	Poor with later fall

At the Henry Ford Hospital one of us (H. N. H.) performed experiments that will be reported in detail elsewhere in which an attempt was made to measure the amount of saline which when infused in the presence of shock will leak out into the local area of trauma. It is known, as seen in Chart 1, that when one hind of limb of a dog is traumatized, about 4.2 per cent body

weight of plasma-like fluid is lost into the limb up to the time of death, as shown by Parsons and Phemister<sup>81</sup> (1930). Similar mechanical trauma, followed by intravenous infusion of 1,980 cc. of normal saline solution, resulted in an excess in weight of 6.3 per cent body weight indicating that about 16 per cent of the infused saline leaked out into the local area of trauma. Because of the small amount of urine (160 cc.) and the low bleeding volume (2.5 per cent body weight), the rest of the saline must have escaped into the tissues generally throughout the body. In other similar experiments, the excess in weight of the traumatized limb in saline treated dogs was as much as 10 per cent body weight. As seen in Chart 2, saline also leaked out into

<b>EXPERIMENT:</b>	
<b><u>TRAUMA + SALINE (4-19-40)</u></b>	
<b>DOG WEIGHT= 15.0 KGM.</b>	
<b>TRAUMA 5:05 P.M.</b>	
<b>GIVE 1980 c.c. SALINE</b>	
<b>BLEED TO DEATH AT 2 A.M.</b>	
<b>BLEEDING VOLUME= 375 c.c.</b>	
<b>(=2.5% B.W.)</b>	
<b>URINE = 160 c.c.</b>	
<b>EXCESS WGT. TRAUMATIZED SIDE</b>	
<b>= 950 GM. (=6.3% B.W.)</b>	
<b>(UNTREATED DOG EXCESS= 4.2% B.W.)</b>	
<b>∴ 2.1% B.W.= 315 c.c. OF SALINE</b>	
<b>GIVEN WAS LOST LOCALLY AT SITE OF</b>	
<b>TRAUMA, OR ONLY 16% OF TOTAL.</b>	

CHART 1.—In this typical experiment, it is demonstrated that when one side of an anesthetized animal is traumatized and saline is afterward given intravenously, the traumatized limb exceeds the opposite normal limb by an amount equaling 6.3 per cent body weight. When compared with the average 4.2 per cent body weight excess of similarly traumatized limbs not treated with saline, it is seen that about 16 per cent of the saline administered leaked out into the traumatized area.

the locally traumatized area in a case of shock due to subcutaneous bile salt injection. In Chart 3, it is seen that even whole blood when transfused probably causes some increased fluid to leak into the traumatized area. The fact that 37 per cent of the injected volume did so, as opposed to only 16 per cent in the two illustrative saline injection cases, is not taken to mean that blood is more likely to leak out in the locally traumatized area than saline. Rather it is linked up with the smaller absolute volume of blood given and also it is considered to mean that less of the fluid is lost away from the site of trauma.

## (2) GLUCOSE SOLUTION

Practically all of the objections to saline apply equally well to glucose. Murphy, Correll, and Grill<sup>78</sup> (1941), in studying the effects of intravenous



solutions in patients with and without cardiovascular defects, observed dangerous reactions after the use of 50 per cent glucose solution.

### (3) GUM ACACIA SOLUTION

Colloid solutions were used intravenously by Czerny<sup>32</sup> (1894). Hogan<sup>52</sup> (1915) made the first clinical use of these substances, injecting 2.5 per cent gelatin solution. Gum acacia was used clinically by Hurwitz<sup>58</sup> (1917) and

<b>EXPERIMENT (6-28-40)</b>	
<b>SUBCUTANEOUS BILE + SALINE</b>	
<b>DOG WEIGHT = 11.7 KGM.</b>	
<b>INJECT BILE 4.25 P.M.</b>	
<b>GIVE 2575 c.c. SALINE</b>	
<b>DEATH ABOUT 2 A.M. (6-30-40)</b>	
<b>WATER PER OS = 1100 c.c.</b>	
<b>URINE = 3310 c.c.</b>	
<b>EXCESS WGT. INJECTED SIDE</b>	
<b>= 850 GM. (= 7.3% B.W.)</b>	
<b>(UNTREATED DOG EXCESS = 3.8% B.W.)</b>	
<b>∴ 3.5% B.W. OR 409 c.c. OF</b>	
<b>SALINE GIVEN WAS LOST LOCALLY AT SITE</b>	
<b>OF TRAUMA, OR ONLY 16% OF TOTAL.</b>	

CHART 2.—In this typical experiment it is seen that about 37 per cent of the blood administered to a traumatized dog leaked out into the local area of trauma.

popularized by Bayliss<sup>7</sup> (1917). Since then it has been used by many, but recently adverse reports as to its toxic effects have been written by Dick, Warweg, and Andersch<sup>36</sup> (1935); Christie, Phatak, and Olney<sup>29</sup> (1935); Studdiford<sup>90</sup> (1937); Hall<sup>45</sup> (1938); Cattell<sup>25</sup> and associates (1939), and by Hendrick, Keeton, and Foley<sup>60</sup> (1938). Extensive deposition in the liver is one of the drawbacks of acacia. Acacia may remain in the body for months as shown by Andersch and Gibson<sup>4</sup> (1934), or even for years as demonstrated by Keith, Power and Wakefield<sup>59</sup> (1935).

In the controlled experiments of Buttle<sup>24</sup> and associates (1940) on cats, three different samples of gum acacia solution were tested. Immediate recovery in all the animals was good, but there was a tendency for the blood pressure to fall after the infusion ended and three, of the eight animals tested, died. The fall of blood pressure may be explained in part by the fact that acacia leaves the blood stream easily as claimed by Amberson<sup>3</sup> (1937), but Buttle<sup>24</sup> and associates believe it is more likely due to specific action of the gum on the vessels causing dilatation and increased capillary permeability as originally claimed by Drinker<sup>38</sup> (1927). Buttle<sup>24</sup> and his coworkers con-

cluded that "the effects of gum-saline were much better than those of saline or glucose, but were not as good as those of whole blood."

#### (4) GELATIN-SALINE SOLUTION

This method was used by Hogan<sup>52</sup> (1917) and was recently revived by Chambers<sup>26</sup> (1941) in his experimental studies. It may prove of value in the future.

<b>EXPERIMENT:</b>	
<b><u>TRAUMA + TRANSFUSION (3-1-40)</u></b>	
DOG WEIGHT = 20.4 K G M.	
TRAUMA 4:41 P.M.	
GIVE 780 c.c. BLOOD	
DEATH AT 1:05 A.M.	
BLEEDING VOLUME (BLALOCK) = 175 G.C.	
( = 0.85 % B.W.)	
URINE = 0	
EXCESS WGT. TRAUMATIZED SIDE	
= 1150 GM. (= 5.6 % B.W.)	
(UNTREATED DOG EXCESS = 4.2 % B.W.)	
= 1.4 % B.W. OR 286 c.c. OF	
BLOOD GIVEN WAS LOST LOCALLY AT SITE	
OF TRAUMA, OR ONLY 37 % OF TOTAL.	

CHART 3.—In this typical experiment, it is seen that about 16 per cent of the saline administered to an anesthetized dog with shock due to subcutaneous bile injection leaked out into the local area of trauma.

#### (5) AMINO-ACID SOLUTION

Several articles refer to this solution, but since a casein hydrolysate is used in most cases, this will be considered in the next section.

#### (6) CASEIN DIGESTATE

Casein is used because it contains all of the 11 essential amino-acids. Elman and Weiner<sup>41</sup> (1939), Farr, Emerson, and Fletcher<sup>44</sup> (1940), and Elman<sup>42, 43</sup> (1940) in two papers discussed this mode of therapy. Madden, Zeldis, Hengerer, Miller, and Whipple<sup>68</sup> (1941) and later Madden<sup>69</sup> (1941) studied the utilization of a casein digestate injected by vein in forming plasma proteins. By an established technic for the measurement of plasma protein production in hypoproteinemic dogs, these authors determined that an enzymatic (papain) digest of commercial casein (Lilly) given parenterally is as effective in plasma protein production as whole liver by mouth. The golden yellow granular material containing 12.5 per cent protein is made into a 5 per cent solution and when given either intramuscularly or subcutaneously is well-tolerated. As much as 16 Gm. of the digestate was given in four minutes. These authors concluded that "certain *digests* given by vein or subcu-

taneously *promote new plasma production* as effectively as protein fed by mouth." (Italics are those of Madden,<sup>68</sup> *et al.*)

#### (7) ASCITIC FLUID

Ascitic fluid was used experimentally in shock treatment by Davis and White<sup>35</sup> (1938), Choisser and Ramsey<sup>27, 28</sup> (1938, 1939), and by Mulder, Davis, and Streeter<sup>77</sup> (1939). This latter group of authors applied the lyophile principle of ascitic fluid, redissolving the dried fluid in water and injecting it in, usually, a two and one-half times original concentration. Maes and Davis<sup>70</sup> (1941) have recently reported on the use of ascitic fluid in 22 transfusions in human beings with good results. Providing that enough ascitic fluid is available, this method of treatment may prove of value in the future.

Holubec<sup>54</sup> (1940) stated that Meerson and Čukanowa (1936) had already reported the clinical use of ascitic fluid transfusions in 60 cases. Holubec<sup>54</sup> used as donor a patient age 42 with mitral stenosis. The ascitic fluid had a specific gravity of 1.019 and was used with good results in combination with preserved blood in the treatment of five cases of shock.

#### (8) WHOLE BLOOD

Papers on this subject are so numerous that only the reviews of V. Ziemssen<sup>97</sup> (1892), Rossius<sup>85</sup> (1925), Doan<sup>37</sup> (1927), Vary<sup>91</sup> (1940), Harkins<sup>46</sup> (1941), and Hoxworth and Skinner<sup>56, 57</sup> (1941) will be cited. Several types of blood are usable:

(a) *Direct transfusion*.—This type of administration is valuable, but its practical difficulty outweighs any theoretical advantage it may have. In time of war its usefulness is still further narrowed.

(b) *Citrated fresh blood*.—This blood has great usefulness, but in time of war is not as valuable as:

(c) *Citrated preserved blood*.—With modern methods of blood preservation, as discussed in the review of Harkins<sup>46</sup> (1941), this type of blood more than makes up in practicability any theoretical disadvantages it may have.

(d) *Placental blood*.—This type of blood can never be used on the large scale demanded by wartime. Placental blood samples are, furthermore, frequently infected.

(e) *Cadaver blood*.—This method is especially used in Russia by Youdine<sup>96</sup> (1936). One of us (H. N. H.) visited Professor Youdine's clinic in 1939 and saw cadaver blood transfusions in actual use. The reaction rate is slightly higher than with citrated blood and the method also requires a larger number of fresh cadavers than is found in a single hospital in practically any city in this country.

*Importance of hemoglobin*.—Another point to consider in choosing between different methods of shock treatment is the relative importance of the quantitative reduction in blood volume and any qualitative alteration in the patient's hemoglobin content. Brodin and Saint Girons<sup>20</sup> (1939) believed

that the blood volume decrease and not the anemia is of prime importance in shock. Maes and Davis<sup>70</sup> (1941) have emphasized the relative unimportance of lack of hemoglobin itself in cases of shock. In advocating ascitic fluid injections they stated: "Despite the fact that ascitic fluid contains no hemoglobin, its use in states associated with acute loss of whole blood is rational, as in such states there is usually enough hemoglobin remaining to carry on the respiratory functions of the blood. Only 3 Gm. of hemoglobin per 100 cc. of blood is necessary to maintain adequate oxygenation in the mammalian organism." To draw a simile, if a traffic jam has interfered with transport of food to a starving town, it is much more important to enable the trucks present to move more rapidly than to add more trucks. Thus, if in shock the blood flow is reduced to one-fifth normal, increasing the red cells by a one-fifth will be only one-twenty-fifth as effective as bringing the blood flow up to normal.

Black and Smith<sup>12</sup> (1941), in discussing the relative merits of whole blood and plasma in the treatment of bleeding peptic ulcer, stated: "In general terms, plasma is contraindicated when the hemoglobin is less than 50 per cent." Some such compromise course as this would seem to be better than advising plasma in all shock cases. In the past two years, the pendulum has swung so far in the direction of using plasma that surgeons pay more attention to what they are injecting than to the needs of the patient. There is much truth to Strumia's statement<sup>88</sup> (1940) that there is only one emergency condition—carbon monoxide poisoning—in which whole blood has a marked advantage over plasma, but extremes should be shunned. Perhaps the best rule for blood substitutes is to actually substitute what is lost. Where blood is lost, give blood; where plasma is lost, give plasma.

TABLE III

## METHODS OF CALCULATING TRANSFUSION DOSAGE

- (1) Method of Elkinton, Wolff, and Lee<sup>40</sup> (1940)  
Based on blood concentration and plasma protein level. Especially applicable to burns
- (2) Method of Bushby, Kekwick, and Whitby<sup>23</sup> (1940)  
Comparing the blood concentration before and after a test plasma infusion
- (3) Method of Hill<sup>51</sup> (1941)  
Comparing the blood concentration before and after a test cell infusion

*Methods of calculating transfusion dosage.*—Several methods have been published of accomplishing this in patients without directly determining the blood volume. The method of Elkinton, Wolff, and Lee<sup>40</sup> (1940) is especially applicable in burns or other instances of pure plasma loss. As seen from Table III, it depends on observation of the hematocrit and plasma protein concentration. The method of Bushby, Kekwick, and Whitby<sup>23</sup> (1940) is also listed in the table. Hill<sup>51</sup> (1941) has another method of measuring the amount of fluid necessary to give in shock. He does this by a simple method of calculating the blood volume which is then compared with the normal blood volume of a patient of that size. The difference between the normal and the

actual blood volumes indicates the amount of fluid that it is necessary to give. The initial blood volume is calculated as follows:

$$\begin{aligned} BV_i &= \text{Initial blood volume} \\ Hb_1 &= \text{Initial hemoglobin of patient's blood} \\ Hb_2 &= \text{Hemoglobin of infused cell solution} \\ Hb_3 &= \text{Final hemoglobin of patient's blood} \\ c &= \text{Volume of cell solution} \\ BV_i &= \frac{c (Hb_2 - Hb_3)}{(Hb_1 - Hb_3)} \end{aligned}$$

The more concentrated the red cell solution is, the more effect a given amount will have and the more accurate the computed result will be. This method is the exact opposite of that of Bushby, Kekwick, and Whitby<sup>23</sup> (1940). The cell solution may be harder to give, but is less apt to leak out and vitiate the results.

#### (9) PLASMA

Buttle<sup>24</sup> and associates (1940), speaking of a 50 per cent hemorrhage stated: "In hemorrhage of this degree replacement of red cells plays no vital part in treatment . . . replacement with plasma gives as satisfactory a result as replacement with whole blood." In their cat experiments, there were no deaths in the plasma treated series and in all instances the blood pressure not only rose to normal but the level was maintained.

Plasma has been used in one form or another for several years and the results have been reported by many writers. Reference will be made to the review by Harkins<sup>46</sup> (1941) for the bibliography, and to the note by Brennan<sup>18</sup> (1941). Plasma is used in several forms, as follows:

(a) *Natural plasma*.—This has the advantage that it can be obtained from blood banks in large quantities. It is especially useful in the treatment of burns. That the use of plasma is not a new idea is testified by quotation of the following letter appearing in the March 9, 1918, number of the British Medical Journal:

#### "TRANSFUSION OF PLASMA

"Sir,—I have been reading with interest recent articles in the Journal on blood transfusion in casualty clearing stations. Apparently one of the chief troubles is the question whether or not the recipient's plasma will haemolyze the corpuscles of the donor.

"Surely this difficulty might be avoided by not transfusing the corpuscles at all, but only citrated plasma, which would be easy to keep and easy to give. There is abundant clinical and experimental evidence that it is not the corpuscles that are wanted, but the ideal fluid for keeping blood pressure at its proper level, and the apparent advantage of blood is, no doubt, due to its permanent value in this respect and to its food value. A man apparently dying from haemorrhage is not dying from lack of haemoglobin, else severe cases of anaemia would die long before they do, but from draining away of fluid, resulting in devitalization and low blood pressure.

"May I at least recommend a trial of this method, controlled, let us say, by an equal number of whole blood transfusions and an equal number of gum acacia (not less than 6 per cent.) cases?—I am, etc.,

"Sevenoaks, March 3

Gordon P. Ward,  
Captain R. A. M. C. (S. R.)."



(b) *Reconstituted normal plasma*.—This is plasma that has been dried and is then diluted with water up to its original concentration. Vaughan<sup>92</sup> (1941) and others have pointed out that when such plasma is filtered and allowed to stand it tends to clot more than unfiltered plasma. The use of dried plasma has recently been reviewed in an editorial<sup>39</sup> in the *Lancet* (1941) and in an article by Harper<sup>47</sup> and coworkers (1941). At the Henry Ford Hospital, we have used reconstituted plasma dried by the rotor pervaporator of Hartman<sup>48</sup> (1940).

(c) *Reconstituted concentrated plasma*.—This is usually given in four times normal concentration.

(d) *Calcificated plasma*.—Clegg and Dible<sup>30</sup> (1940) convert their plasma into serum by adding calcium chloride. Experiments on this conversion at the Henry Ford Hospital indicate that the titration sodium citrate = calcium chloride is not always simple and that this method may lead to uncertain results.

(e) *Heterologous plasma*. The use of bovine plasma in particular has been studied by Cohn<sup>31</sup> (1940) and by Wangensteen, Hall, Kremen, and Stevens<sup>94</sup> (1940). Kremen, Hall, Koschnitzke, Stevens, and Wangensteen<sup>62</sup> (1941) recently reported on their results with administration of bovine plasma intravenously to man. The fluid contained 0.3 per cent sodium citrate and 20 mg. per cent sulfanilamide as a final concentration. It was given after skin tests and gradual desensitization, even in the cases with negative skin tests. With this material in unit doses of 250 cc., 119 patients were treated. Two cases of shock were treated, including a case of bleeding peptic ulcer and as much as 2,500 cc. was given to three cases. There were no deaths, but three anaphylactoid reactions occurred. Savage, Taylor, and Keys<sup>86</sup> (1941) studied the sensitivity to various heterologous plasmas and found that dog and fox plasmas cause most reactions in man of those tested (cow, goat, rabbit, sheep, horse, human, dog, and fox). Cow plasma gave no more positive skin tests than did human plasma. Another point of interest was that just because a person was sensitive to one plasma did not mean that he would be to those of other species.

#### (10) SERUM

The relative merits of serum and plasma are frequently discussed of late. In general, plasma is more apt to develop fibrin deposits, while serum is said to be more toxic. Buttle, Kekwick, and Schweitzer<sup>24</sup> (1940) found, in their controlled experiments on cats in which plasma effected recovery, serum caused only a temporary improvement in blood pressure. Furthermore, a severe reaction occurred in five out of seven cats. Such reactions after serum were noted by Brodie<sup>19</sup> (1900). Buttle<sup>24</sup> and associates concluded that "some toxic substance absent from plasma was present in serum." The literature on the question of liberation of physiologically active substances in serum was reviewed by Amberson<sup>3</sup> (1937) who stated: "Blood plasma is to be preferred to serum because of the formation, in the latter, of vasodilator or constrictor

substances produced in the act of clotting." A similar conclusion was reached by Doan<sup>37</sup> (1927), Brodin and Saint Girons<sup>20</sup> (1939), Scudder<sup>87</sup> (1940), and by Strumia, Wagner, and Monaghan<sup>89</sup> (1940).

Serum as opposed to plasma is not without its supporters, however. Its use is favored by Levinson, Neuwelt, Rubovits, and Necheles<sup>65, 66</sup> (1940); Clegg and Dible<sup>30</sup> (1940), and by Brown and Mollison<sup>22</sup> (1940). Concentrated serum was used in burn treatment by Qvist<sup>83</sup> (1941). In his recent Greensfelder Lecture, Blalock<sup>16</sup> (1941) pointed out that at present the shift is toward the use of serum.

At present, very little natural serum is used and as far as we are aware, no heterologous serum has been administered clinically. Main emphasis has been placed upon reconstituted dried serum, either in the normal or concentrated form. Serum has been used by Aldrich<sup>2</sup> and associates (1938), Bond and Wright<sup>17</sup> (1938), Lehman<sup>64</sup> (1939), and others cited above. Brown<sup>21</sup> (1941) was unable to confirm the results of Aldrich<sup>2</sup> and associates (1938) on the value of concentrated serum in nephrosis.

Hill, McMichael, and Sharpey-Schafer<sup>50</sup> (1940) found that, as already cited, crystalloid solutions increase the blood volume only temporarily in normal persons or in shocked patients. On the other hand, they stated that: "Serum given intravenously to normal people is retained in the circulation for long periods. The rise in blood volume depends on the total quantity of protein added, and is independent of the dilution of the serum employed," and "Intravenous serum is very effective in overcoming circulatory collapse due to diminished blood volume."

#### (11) RED CELL SOLUTION

Buttle<sup>24</sup> and associates (1940) injected a red cell suspension into cats in their controlled experiments. The immediate recovery after transfusion was good, but the blood pressure tended to fall and respiration was much disturbed in all experiments. Three of the six animals died. Rossius<sup>85</sup> (1925) reported that red cells exert about the same resuscitating power as saline in the treatment of acute hemorrhage. It would seem advisable, at present, to reserve the use of red cells left over in blood banks for treatment of chronic anemic states rather than of acute traumatic shock. Mollison<sup>76</sup> (1941) advised against the use of red cell solutions of over seven and one-half million cells per cubic mm. because of the factor of increased viscosity.

#### (12) HEMOGLOBIN-RINGER SOLUTION

This solution has been mainly used for experimental purposes. Amberson<sup>3</sup> (1937) stated that it has the following advantages as a blood substitute: It exerts a high colloidal osmotic pressure and the dissolved hemoglobin takes up oxygen and stimulates hematopoiesis. Buttle<sup>24</sup> and his associates (1940) used a solution containing 3.7 Gm. of oxyhemoglobin per 100 cc. The immediate recovery of the blood pressure was good, but there was a tendency for it to fall during the period of observation and to be highly unstable. Respira-

tory disturbances were frequent. These authors concluded that this solution gives uncertain results which are not as good as those of whole blood, but which are better than those obtained with acacia. This solution is also apt to lead to renal tubular occlusion as shown by Amberson (1937), Baker and Dodds<sup>6</sup> (1925) and Aubertin<sup>5</sup> and his colleagues (1939). The use of hemoglobin-Ringer solution in four patients with anemia was reported by O'Shaughnessy, Mansell, and Slome<sup>80</sup> (1939). After preliminary alkalinization of the urine, amounts of 200, 250, 600, and 1,000 cc. of 5 per cent solution were given intravenously in an hour or less to four patients respectively.

## CONCLUSIONS

(1) Saline and glucose solutions are unsuitable for blood substitutes because they are lost so quickly from the damaged vessels.

(2) Plasma and serum are at the present time the best substitutes for whole blood and in some cases are better than blood itself. In cases of marked anemia, whole blood is preferable.

(3) Use of ascitic fluid, bovine plasma, and casein digestates may be of value in the near future, but such use is still in the experimental stage.

(4) Adequate dosage computed by the methods outlined in the paper, or by similar means, is essential.

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## CLINICAL SIGNIFICANCE OF PROTHROMBIN DEFICIENCY AND ITS TREATMENT

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THE DISCOVERY of vitamin K has led to renewed interest in the mechanism of blood clotting, a field of study which for years has baffled many investigators. Indirect methods for the measurement of plasma prothrombin concentration have been developed, and as a result the clinical importance of prothrombin deficiency has also been brought under study. According to current ideas, plasma prothrombin, ionized calcium, and a tissue or platelet factor, thromboplastin, interact in the first phase of clotting with the formation of thrombin. Thrombin then acts upon plasma fibrinogen and fibrin is laid down. The process is known to be influenced by temperature,  $p_H$ , electrolyte pattern, and colloid content of the medium, as well as the concentration of the four primary clot factors. The nature and mode of action of the physiologic anticoagulants is as yet undetermined, but there is good reason to suppose that such substances exist and that their effect may be exerted against either or both of the two phases of clotting. The place of heparin in physiologic clot inhibition and the manner in which it acts are questions still unanswered, though the subject is being intensively investigated.

It has not been determined to what extent clotting is an enzyme reaction, and, indeed, the nature of the clotting mechanism must stand in clear relief before such intimate analysis will be possible. There can be no doubt, however, that the speed of clotting under physiologic conditions is directly related to the concentration of thrombin. The concentration of thrombin further depends on the concentration of prothrombin, though variables come into consideration at this point. The speed of formation of thrombin from prothrombin is influenced by concentration of thromboplastin, ionized calcium and antiprothrombic agents, and possibly by inherent "convertibility" of the individual's prothrombin,<sup>1, 2</sup> a rather vague conception. The rapidity of clotting is obviously of the utmost importance in determining the hemostatic value of the process, but a neglected subject, of equal or greater importance, concerns the factors affecting the quality of the formed clot. Those who have worked with plasma clotting, in which the gross physical characteristics of the clot can be readily observed, know that the fibrin mass may be soft and jelly-like, tough and opaque, adherent or slippery, granular, friable, or noncontractile. These qualities are not necessarily related to the speed of clotting, but probably depend in part, at least, on the concentration and quality of the fibrinogen.

*Methods of Measuring Plasma Prothrombin Concentration.*—Though knowledge of the coagulation reactions is incomplete, nevertheless, there can be no doubt about the clinical value of prothrombin determinations as performed by recently developed methods. As previously noted, these methods are indirect, for prothrombin cannot be isolated and weighed, or brought into definite measurable chemical combinations. The two methods which, in their original or modified forms, have been most widely used in this country are the two-stage titration method of Warner, Brinkhous, and Smith,<sup>3, 4</sup> and Quick's method of measuring clotting time of plasma in the presence of optimal concentration of calcium and thromboplastin.<sup>5, 6</sup> The first is more complicated, but results in better control of the variables and yields more precise data. The two-stage technic is preferable in investigative work, while Quick's method is more practical in controlling the administration of vitamin K clinically. Quick's method has been variously modified by using sodium citrate as the anticoagulant instead of sodium oxalate, by varying the amount of calcium chloride used in recalcification, by using thromboplastin from different sources, by serial dilution of the plasma, and by expressing the results in different terms. It should be borne in mind in using the Quick method that a linear relationship does not exist between prothrombin concentration and the plasma clotting time, and that it is, therefore, not permissible to convert clotting time directly into percentage of the normal control value. The "bedside method,"<sup>2</sup> in which the determination is made on freshly drawn whole blood, thus obviating the use of anticoagulants and the centrifuge, in the author's experience, gives rather variable results, though it yields more significant information than does the ordinary determination of clotting time. Methods have been proposed for studying the prothrombin content of infants' blood which avoid the need for venepuncture by using small amounts of blood from a stab wound, and apparently such methods yield clinically helpful data.<sup>7, 8</sup>

*Occurrence of Prothrombin Deficiency.*—An examination of the known facts of vitamin K metabolism suggests clinical and experimental states in which the normal rôle of this accessory food factor may be disturbed. Vitamin K occurs naturally as a fat-soluble substance or substances, rather widely distributed in leafy green vegetables and in certain animal tissues. Its proper absorption, like that of other fat-soluble vitamins, depends on the presence of sufficient amounts of bile salts in the small intestine. Absorption from the colon probably does not occur. After absorption from the intestine vitamin K conditions, in some as yet unknown manner, the formation of prothrombin by the liver. Prothrombin is a constituent of the plasma globulin, and apparently both vitamin K and prothrombin are not stored to any significant extent in the body. From this one might expect prothrombin deficiency as a result of insufficient intake of vitamin K, lack of bile salts in the intestine with or without jaundice, impaired absorption of nutrients from the intestine as in diarrheal states, and defective digestion and absorption of fat due to lack of pancreatic enzymes. In addition, prothrombin deficiency might, theoretically, be based on impaired liver function from intrinsic liver disease, with conse-

quent failure in utilization of vitamin K. Prothrombin deficiency has in fact been encountered clinically in most, if not all, of these circumstances.

It was discovered early in the investigation of vitamin K that a number of the common bacteria, such as *E. coli*, *Staphylococcus aureus*, *B. subtilis*, the *Mycobacterium tuberculosis* synthesize the substance.<sup>9</sup> Bacterial synthesis of vitamin K was further found to take place normally in the intestine of mammals and fowls, presumably distal to the mucosal areas in which absorption occurs. In the production of K-avitaminosis in chicks by dietary restriction, Almquist and Stokstad found it necessary to keep the chicks from access to their droppings, as otherwise deficiency did not develop.<sup>10</sup> These points may be of significance in relation to the occurrence of hypoprothrombinemia in the newborn before the intestinal bacterial flora has been established, though the mechanism is not entirely clear.

Prothrombin deficiency is commonly present in obstructive jaundice, and in this condition poor absorption of vitamin K and impairment of hepatic synthetic power may be present in combination.<sup>11</sup> In a group of 50 cases of obstructive jaundice, which have come under the author's observation at the Massachusetts General Hospital, the plasma prothrombin concentration was invariably reduced before treatment, the average value in the cases of calculous obstruction being 65 per cent, and in the cases of carcinomatous obstruction 45 per cent. In every case, the prothrombin value improved after administration of vitamin K parenterally or vitamin K and bile salts orally, though the patients with calculous obstruction responded better, probably owing to greater hepatic functional reserve. In a group of 112 patients with obstructive jaundice operated upon at the Massachusetts General Hospital during the six-year period, 1931 to 1936 inclusive, 15 per cent died of massive postoperative hemorrhage. In the author's experience, the proper use of vitamin K before and after operation, together with adequate nutritional therapy, has entirely eliminated this hazard, even in patients with severe liver damage and initial prothrombin concentrations below 10 per cent.

It has been shown that an immediate postoperative reduction in plasma prothrombin concentration is the rule after operation for obstructive jaundice.<sup>12, 13, 14</sup> The reduction may be as great as 30 or 40 per cent, and occurs most commonly within the first four days, from which the need for having the preoperative prothrombin value well above the hemorrhagic zone is apparent. The depression may follow spinal or local anesthesia, and probably is due to the hepatic trauma and blood loss of operation, as well as absence of prothrombin reserves. After operations for conditions other than obstructive jaundice, and in patients without liver disease, postoperative hypoprothrombinemia does not seem to occur.<sup>12</sup> In the early experiences with the clinical use of vitamin K, when only the crude alfalfa meal extracts and bile salts were available for oral treatment, the author observed two instances in which patients refused to take the material after operation for obstructive jaundice. The interesting point was that following the resultant massive wound hemorrhage a further reduction in plasma prothrombin concentration immediately



occurred, from which one is led to believe that hemorrhage may be a contributory factor in exhausting a depleted plasma prothrombin content.

Prothrombin deficiency may occur in acute hepatitis, such as "catarrhal jaundice," though usually the reduction is moderate. The hypoprothrombinemia is not proportionate with the jaundice, and this gives the determination value in the differential diagnosis of jaundice from intrahepatic disease and from extrahepatic block. In the progression of acute hepatitis to acute yellow atrophy or liver failure, however, the plasma prothrombin concentration falls to values in the hemorrhagic range, which is below 40 per cent.<sup>16</sup> Cirrhosis of the liver may be accompanied by moderate reduction in plasma prothrombin concentration, and in patients with bleeding esophageal varices the value may be less than 40 per cent. It is reasonable to suppose that in such cases the clotting defect may be a contributory factor and may lead to gross rather than microscopic bleeding from a lesion exposed to constant trauma.

Of special surgical interest is the group of cases in which toxic hepatitis, jaundice, and massive hemorrhage follow operation for peritoneal infections, such as perforative appendicitis, ruptured peptic ulcer, subdiaphragmatic abscess, and pelvic abscess. These complications seem to be more common when peritoneal sepsis is of gastro-intestinal origin, and determination of plasma prothrombin concentration as well as serum protein concentration should be routinely and periodically performed in the care of patients with such infection.<sup>15</sup> The reduction in plasma prothrombin may develop rapidly and to an extreme degree. The resulting clotting defect may not only cause massive hemorrhage from operative wounds, but may retard inflammatory fixation and exudative confinement of the infection.

Reduction in plasma prothrombin concentration may be encountered during the administration of sulfanilamide, sulfapyridine and sulfathiazole in the treatment of infection. These drugs are known to exert a toxic effect on the liver, and presumably the hypoprothrombinemia comes from depression of liver function. Severe acute infections, however, may lead to reduction in plasma prothrombin concentration in the absence of chemotherapy, and the deficiency may be refractory to vitamin K treatment.<sup>16</sup> Depression in plasma prothrombin has been observed to precede jaundice as an early indication of hepatitis in the chemotherapy of infections, and the determination should be freely used in the control of such therapy. At the same time the importance of nutritional measures directed at maintaining hepatic reserve, such as high carbohydrate and high vitamin intake and blood transfusions, during the management of chemotherapy is brought into focus.

Severe hypoprothrombinemia may develop in chronic external biliary fistula, if the patient does not take adequate amounts of bile salts orally in replacement. The author has seen near-fatal intracranial hemorrhage in two patients who failed to take the prescribed amount of bile salts and vitamin K following the surgical formation of external biliary fistula. The patients were middle-aged women without arteriosclerosis or hypertension, and in both

there was much reduction in hepatic reserve. The prothrombin concentration at the time of hemorrhage was below 10 per cent, and the bleeding was readily controlled by giving vitamin K parenterally. In a third case of complete external biliary fistula of 14 months' duration, there was unaccountable absence of the bleeding tendency and only moderate reduction in plasma prothrombin, even though the patient had had no dietary or replacement therapy. In this connection, it is worth remembering that the bile drained through an external fistula in the presence of liver damage, may have a low bile salt content, and hence may have little value in digestion and absorption. The cholic acid content of such bile should be determined, or else refeeding of the bile should not be practiced. In any event, cholic acid derivatives in capsule or tablet form are much more easily taken than a bacteria-laden, nauseating liquid.

Some doubt exists as to whether prothrombin deficiency can occur in man purely on the basis of insufficient intake of foods containing vitamin K. Scarborough concluded from a study of 18 patients showing outspoken evidence of scurvy, beriberi, or pellagra that the prothrombin values in the plasma were normal as determined by Quick's method.<sup>17</sup> On the other hand, Kark and Lozner,<sup>18</sup> in studying four patients with clinical hypovitaminoses, found low plasma prothrombin values by a method of serial dilution of the unknown plasma with prepared prothrombin-free normal plasma. The question is rendered difficult by uncertainties as to liver function, bile salt excretion, and alterations in mucosal absorbing power in patients suffering from severe nutritional disturbances. In the author's experience, patients undergoing elective surgical operation and without clinical evidence of malnutrition frequently show moderately reduced plasma prothrombin values both by the method of Warner, Brinkhous, and Smith, and by Quick's method. For this reason normal control plasma must be selected with care. It remains to be shown, however, that a clinically significant degree of hypoprothrombinemia occurs in man purely from vitamin K lack.

Failure in absorption of vitamin K is to be expected in any condition in which the digestion and absorption of fat is seriously impaired.<sup>19</sup> Idiopathic steatorrhea without evidence of liver disease may lead to spontaneous hemorrhage and hypocalcemic tetany from lack of vitamin K and vitamin D.<sup>20</sup> Prolonged hyperactivity of the intestine may result in prothrombin deficiency from poor absorption of vitamin K, as in chronic ulcerative colitis.<sup>28, 19, 21</sup> Following parenteral injection of vitamin K in this condition, improvement in prothrombin concentration and diminution in bleeding from colonic ulcers has been observed.

There is abundant evidence now on record indicating the importance of prothrombin deficiency as a factor in hemorrhagic disease of the newborn.<sup>22, 7, 23, 24, 25</sup> Brinkhous, Smith, and Warner observed a uniform reduction in the plasma prothrombin levels in the newborn and throughout infancy.<sup>22</sup> During the first 11 days, values ranging from 26 to 44 per cent of normal were found, and thereafter there was a gradual rise until a nearly normal level was reached at the end of ten and one-half months. Maternal

prothrombin values, before and after delivery, were normal. As determined by Quick's method, plasma prothrombin in the newborn is apparently less commonly found reduced,<sup>26</sup> though prolongation of the prothrombin time can often be demonstrated from the first to the sixth day. The discrepancy in the findings by the two methods has led to the suggestion that the available prothrombin in the newborn has a higher "convertibility" than in the adult,<sup>26</sup> which would tend to compensate for the deficiency in the newborn. Mounting clinical evidence leaves no doubt as to the existence of profound hypoprothrombinemia in the newborn with hemorrhagic disease, and the response to the parenteral administration of vitamin K is dramatic and lifesaving. The rapidity of response suggests that the cause of the deficiency is lack of vitamin K rather than primary hepatic dysfunction, though the pathogenesis of the condition requires further study. Of similar significance is the finding that plasma prothrombin values in the newborn are much higher than average if the mother is given vitamin K before delivery, and this is true even if the maternal plasma prothrombin concentration is normal before the administration of vitamin K.<sup>27</sup>

Hemorrhagic states into the etiology of which prothrombin-lack does not enter are thrombocytopenic purpura, hemorrhagic retinitis, aplastic anemia, leukemia, polycythemia vera, hemophilia, and multiple congenital telangiectases.<sup>28, 5</sup> In any case of bleeding of doubtful etiology, the prothrombin concentration of the plasma should be determined, but if the value is within normal limits no benefit is to be expected from vitamin K therapy.

*Effects of Prothrombin Deficiency.*—It should be borne in mind that the extent of hemorrhage resulting from tissue trauma depends on the summation of opposing reactions. The cross-sectional area of the wound in the vascular bed, the size and contractility of the vessels laid open, the mobility and temperature of the part, the force of the blood pressure, and the richness of the local tissue thromboplastin supply are variables independent of the quality of the circulating blood, which, nevertheless, influence the success of the hemostatic process. From these considerations, it is clear that the clinical manifestations of prothrombin deficiency may be expected to vary greatly. Given absolute freedom from injury, no demand would be made on the hemostatic defenses, and complete absence of plasma prothrombin might pass unnoticed. The patient with obstructive jaundice and severely reduced plasma prothrombin concentration may get along without serious hemorrhage until surgical incision is made in the abdominal wall, as was repeatedly shown in clinical experience before the discovery of vitamin K. Likewise, the danger of hemorrhage from a lesion constantly exposed to trauma, such as duodenal ulcer, ulcers of chronic ulcerative colitis, and esophageal varices becomes greater as the clotting mechanism is crippled by lowering of plasma prothrombin concentration.

It is of interest to consider the reported sites of hemorrhage following operation in patients with obstructive jaundice treated before vitamin K was discovered. This is the group of patients in whom prothrombin deficiency is

most constant and severe, for a combination of etiologic factors is at work, such as lack of bile salts in the intestine, intrinsic liver damage, infection and, often, inadequate dietary intake. Bleeding into excoriated skin, nosebleeds, and bleeding from gums were not unusual. Severe postoperative bleeding, however, occurred into the wound, the gastro-intestinal tract, the peritoneal and pleural cavities, skeletal muscles, the urinary passages, and sometimes into the uterine canal. Hemoptysis and hemarthrosis were rare.

In a group of untreated patients with obstructive jaundice which came under the author's observation during the past three years, tests for blood in the stools were frequently positive. In nine of 22 patients with calculous obstruction of the common duct, and in 13 of 22 with neoplastic obstruction the guaiac test on the stools was strongly positive, and the test became negative under vitamin K therapy before operation, coincident with improvement in plasma prothrombin concentration. No ulcerations were visible in roentgenologic studies of the gastro-intestinal tract, so one is led to suppose that the bleeding was from small excoriations of the mucosa.

Petechial hemorrhage is uncommon in prothrombin deficiency, though small hemorrhages into cutaneous abrasions produced by scratching are frequently present in patients with obstructive jaundice. Numerous and large ecchymotic areas were observed over the trunk in a patient with idiopathic steatorrhea and plasma prothrombin values below 15 per cent. Epistaxis and bleeding from the gums may occur in prothrombin-lack. Reference has already been made to two patients with chronic external biliary fistula who had severe intracranial hemorrhages as a result of neglecting bile salt and vitamin K therapy. The author has seen hemoptysis from lung abscess and uterine hemorrhage from hyperplastic endometritis associated with plasma prothrombin concentrations of 65 to 75 per cent, but the importance of the hypoprothrombinemia in such cases is open to question. A group of 30 patients with chronic pulmonary tuberculosis were found to have moderate hypoprothrombinemia, but the values were no lower in the patients having hemoptysis. Bleeding into the urinary tract is rare in prothrombin-lack in the absence of adequate local causes, but such clotting deficiency may perhaps occasionally be a contributory factor.

A consideration, possibly of great importance, is the rôle of plasma prothrombin in resistance to infection. The thrombosis of lymphatics and capillaries at the boundary of an inflammatory process and the coagulation of plasma exudate in the region presumably would be impaired by prothrombin deficiency, although the direct conversion of fibrinogen into fibrin by bacterial or inflammatory products might operate in compensation. When large blood vessels become involved in advancing necrotizing infections, the rapid formation and organization of a firm thrombus in response to endo-arteritis is of lifesaving importance.

The characteristic peritoneal reaction to trauma is capillary dilatation and transudation of plasma, with the formation of a plastic exudate. The surgeon's suture line after gastro-intestinal operation is quickly sealed over in this

manner, thus initiating fibroblastic healing, and at the same time preventing bacterial leakage. The efficiency of this reaction, on which the safety of abdominal surgery depends, probably is influenced by various factors, but of unquestionable importance is the plasma content of prothrombin and fibrinogen. The formation of excessive peritoneal adhesions after peritoneal trauma may arise in factors which exaggerate this vital protective process.

*Hyperprothrombinemia.*—The possible occurrence of hyperprothrombinemia, either spontaneously or in response to vitamin K therapy, has been subjected to study. In examining normal individuals and a large number of patients with a variety of diseases, the author has seen only three instances in which the plasma prothrombin concentration, as determined by a slightly modified two-stage method,<sup>28</sup> was above 110 per cent. In one of these patients dehydration was present, as evidenced by elevated plasma protein concentration, and this was adequate explanation for the hyperprothrombinemia. The other two patients were afflicted with a tendency to recurrent thromboses of peripheral veins without any satisfactory explanation. It is possible that in the latter patients a hyperactive clotting mechanism was of pathologic importance. There appears to be no danger of producing hyperprothrombinemia from administering excess of vitamin K and, of course, it is generally true of vitamin therapy that many times the effective dose can be taken without harm. The author has given convalescent surgical patients with normal prothrombin values up to ten times the effective oral dose of vitamin K without ill effects and without elevating the plasma prothrombin concentration above 100 per cent.

*Prothrombin Determination as a Liver Function Test.*—Since plasma prothrombin is formed chiefly if not entirely in the liver, it is not surprising that factors interfering with hepatic function result in depression of the plasma prothrombin concentration. Experimental and clinical evidence indicates that reduction in the prothrombin value may be an early and sensitive index of decline in hepatic reserve.<sup>29</sup> After chloroform anesthesia in patients or in animals, the first detectable sign of the hepatotoxic action of the drug is a sharp reduction in plasma prothrombin concentration.<sup>14, 3</sup> In patients with hypoprothrombinemia, the improvement in the prothrombin value following a single adequate dose of water-soluble vitamin K given parenterally may be used as a liver function test.<sup>30</sup> In patients with liver failure and prothrombin deficiency massive doses of vitamin K given parenterally or orally with bile salts may be without benefit, though complete absence of response indicates extremely severe hepatic change.<sup>16</sup> Intercurrent infection, such as pneumonia or cholangitis, may produce immediate lowering of plasma prothrombin concentration in a patient receiving a daily adequate dosage of vitamin K.<sup>11, 12</sup> The lability of plasma prothrombin concentration makes it important to determine the value frequently and regularly in the management of cases of obstructive jaundice.

*Treatment of Prothrombin Deficiency.*—Before the isolation and identification of the chemical nature of vitamin K in 1939, only crude extracts obtained



from spinach, alfalfa meal, putrefied fish meal, *etc.*, were available for use in treatment. The crude extract was given orally with bile salts, and the efficacy of the therapy is attested to by many clinical and experimental data. Through the efforts of Dam,<sup>31, 32</sup> Almquist,<sup>33, 34, 35</sup> Doisy and his colleagues,<sup>36, 37</sup> Fieser<sup>38, 39</sup> and others, a number of 1,4-naphthoquinone derivatives have been shown to have high vitamin K potency when given in chemically pure form. Vitamin K activity is found in various naturally occurring mono- or di-alkyl 1,4-naphthoquinone compounds, including vitamin K<sub>1</sub> derived from spinach and vitamin K<sub>2</sub> from putrefying fish meal. One of the most potent vitamin K substances studied to date is 2-methyl-1, 4-naphthoquinone, and there is a growing tendency to express the value of other materials in terms of this substance, rather than in the uncertain and variable units proposed earlier by different investigators.

The known naturally occurring vitamin K substances are fat-soluble, and clinical needs led to a search for water-soluble substances which could be more easily administered. A number of water-soluble, highly potent compounds have been identified, as recently described by Fieser, Tishler, and Sampson.<sup>39</sup> These substances can be injected in aqueous solution, or they can be given orally, and they are absorbed from the gastro-intestinal tract in the absence of bile salts.<sup>40, 41</sup> All the known fat-soluble and water-soluble compounds with vitamin K activity have low toxicity, as shown by extensive studies on small animals and in the clinic.

The following methods are available in the administration of vitamin K to patients:

- (1) Crude extracts may be given by mouth, together with bile salts.
- (2) Synthetic fat-soluble vitamin K (2-methyl-1,4-naphthoquinone) may be given by mouth together with bile salts.
- (3) Synthetic fat-soluble vitamin K in oil may be sterilized and injected intramuscularly.
- (4) Synthetic water-soluble vitamin K may be administered by mouth.
- (5) Synthetic water-soluble vitamin K may be sterilized and injected subcutaneously, intramuscularly, or intravenously.

In most instances where the fat-soluble synthetic preparation or the crude extracts are given by mouth, bile salts also should be administered, for even in the absence of jaundice the absorption of the fat-soluble material from the intestines may be facilitated by additional quantities of bile salts.<sup>16</sup> An adequate daily dose is 2 to 4 mg. of 2-methyl-1,4-naphthoquinone or an equivalent amount of one of the other preparations, and it has been found that much larger doses are of no avail if no improvement in the prothrombin concentration follows doses of this size. If bile salts are also being given 1 to 2 Gm. per day is sufficient. In patients with severe liver damage, the author prefers to give vitamin K parenterally and avoid the administration of bile salts. In urgent need, as in the presence of active hemorrhage, vitamin K should be administered parenterally, and the response occurs within a few hours. For patients

who are vomiting, or in whom uncertainty as to absorption exists, the parenteral route should be used.

In the author's experience, hypoprothrombinemia refractory to vitamin K treatment may be encountered in two groups of patients. As already noted, liver function may be reduced to such a point that vitamin K is not properly utilized no matter how generous the supply, or how it is administered.<sup>16, 45, 46</sup> There is also a group of patients with chronic, severe sepsis, such as pyelonephritis, osteomyelitis, or subdiaphragmatic abscess, in whom prothrombin deficiency of moderate degree may exist, and in these patients the deficiency may not respond to vitamin K therapy. In such conditions, blood transfusions are in order, and fresh rather than "bank" blood should be used.<sup>42, 43</sup> The average blood transfusion of 500 cc. may be expected to effect a transitory rise in the adult patient's plasma prothrombin concentration of about 10 per cent.<sup>26, 12</sup>

Since the formation of plasma prothrombin is a function of the liver, it should be borne in mind that an essential part of treatment of prothrombin deficiency consists in the measures known to influence liver function favorably.<sup>44</sup> A high intake of carbohydrate and the proper kind of protein is important, as well as a high vitamin intake. The fluid and electrolyte needs of the patient must be carefully met. In connection with surgical operation, the proper choice of time and anesthesia, and the division of the necessary surgical trauma by two-stage procedures in certain cases are matters for careful consideration, if depleted hepatic reserve is not to be fatally overtaxed.

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## THE TREATMENT OF FRACTURES OF THE HUMERUS BY MEANS OF A HANGING PLASTER CASE—"HANGING CAST"\*

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SINCE 1935, the majority of fractures of the neck and shaft of the humerus have been treated routinely on the Bone and Joint Service of Receiving Hospital by the hanging plaster case.

This encasement was first advocated by Dr. J. A. Caldwell in 1933 for treatment of some fractures of the shaft of the humerus.

The hanging plaster case consists, simply, of a circular plaster bandage which encases the upper extremity from its upper third to the wrist; it holds the elbow in 90° flexion, and is suspended from the neck by a sling.

The plaster bandage is applied with the patient either sitting or recumbent as convenient or as condition of the patient permits, the elbow flexed to a right angle, with the forearm held in midpronation. An adequate length of stockinette is pulled over the arm, and a strip of saddlers' felt, one inch in width, is made to encircle the wrist just above the ulnar styloid. The plaster bandage is applied either with no other padding or with a few turns of flannel bandage.

For adults, four rolls of plaster, four inches by six yards, are used; while three rolls are used for children.

A loop for a sling is made just above the wrist on the upper surface of the encasement by a few turns of the last bandage applied. This loop can be applied either slightly medialward or lateralward to the midline of the upper surface of the encasement to help correct inward or outward angulation of the lower fragment (Fig. 1).

Lateral angulation can be readily corrected by a wedge made of felt, plaster, sponge rubber, or sheet cotton covered with plaster, placed on the inner side of the elbow (Fig. 2). In some cases of fractures of the humeral neck with medial bowing, we have found a roll of sponge rubber, two and one-half inches in diameter, placed high in the axilla and fixed to the encasement, very effective in correcting this deformity (Fig. 3).

The plaster bandage is usually applied after roentgenologic examination. However, when the patient's general condition is not good, or the fragments are found to be in an unsatisfactory position for this method of treatment, these difficulties are first rectified before the encasement is applied.

The patient is instructed after application of the hanging plaster case to allow the arm to swing freely at his side at all times. Many patients have an inclination to rest the elbow on the arm of a chair or some convenient object when sitting. This is contrary to the main purpose of the encasement

\* Since submitting this article we have the results on an additional seventy-six cases which, including those described in an earlier issue elsewhere, make a total of two hundred and fifty-three cases treated in the Bone and Joint Department of the Receiving Hospital, Detroit, Michigan.



which is traction by gravity. This difficulty is greatly lessened when the patient is made to realize the principle of this method of treatment, and that



FIG. 1.—The hanging case showing suspension loop.



FIG. 2.—Showing the sponge rubber roll in position, in order to correct lateral angulation.



FIG. 3.—Showing the felt roll in position, in order to correct medial displacement of the lower fragment.

his chances for a good result depend wholly on his full coöperation.

Some patients find it more comfortable to sleep sitting in a chair for the first week or so; others use a back rest which permits the arm to swing as free as when in the erect position. The remainder sleep satisfactorily with upper arm either resting on a pillow or with the whole arm placed across the chest.

Active motion of the wrist and hand has been encouraged from the beginning. The patient is instructed to lean forward and let the shoulder swing in circular motions several times a day. These passive movements are sufficient to preserve considerable free motion at the shoulder joint until active motion can be safely instituted. After a few days active motion is allowed in the anteroposterior plane. Whenever moderate callus formation can be demon-

strated roentgenologically, active abduction is encouraged.

Roentgenograms are taken two or three days after application of the encasement to determine the position of the fragments, and if necessary, adjustments are then made. From then on until union is adequate to allow removal of the encasement, check-up roentgenograms are taken at two-week intervals.

Fractures of the humerus considered unsuitable for treatment by the hanging plaster case are those that involve the condyles or supracondylar area, badly comminuted fractures of the head with poor position of the fragments, those of the head and neck associated with dislocation at the shoulder joint, and fractures of the greater tuberosity with displacement. These are treated by other methods and none are included in this series.

Since the first report of the results obtained in 58 cases treated by the hanging plaster case in Receiving Hospital by the senior author and Dr. M. G. Rosenbaum, in 1937, the final results of 119 additional cases of the Bone and Joint Service have been observed. This brings the total number of cases, followed from the time they were first seen in the clinic to their discharge, up to 177.

This, however, does not include all cases of the Bone and Joint Service that were treated by this method. Many of these patients failed to return to the clinic for check-up examinations; a number were transferred to other hospitals, or discharged to the care of their family physician, consequently, making it impossible for us to check the end-results.

For uniformity in recording results, the same classification of fractures and terms used to describe the final results obtained in the 58 cases of the first report are again used. This classification is based upon the roentgenographic findings of the injury when first seen: (1) Fractures of the upper third of the humerus—(a) in good or fair position, (b) in poor position. (2) Fractures of the middle and lower thirds of the humerus—(a) in good or fair position, (b) in poor position.

The final results of shoulder function procured upon removal of the encasement or discontinuance of physiotherapy were designated by the terms "excellent," "good," "fair," and "poor." "Excellent" denotes a shoulder which functions almost as well as before injury. Active shoulder abduction to 90° with only slight limitation of external rotation is termed "good." A less degree of function is "fair." "Poor" indicates only slight motion.

There were 49 fractures of the upper third of the humerus in good or fair position (Table I). Of these, the youngest patient was seven years of age and the oldest 85. Hanging plaster encasements were applied in all cases in this group without any previous manipulation. In all, except four cases (Cases 4, 8, 12, and 34) the encasements were put on from a few hours to five days following the injury (Figs. 4 and 5).

Case 4 suffered from a head injury received at the time of the arm injury. She remained in bed for two weeks with the injured arm strapped to her side while convalescing from the skull injury.

Cases 8 and 12 were compound fractures. Case 8 remained in bed for the first five days with the arm in skin traction and a Thomas arm splint. Case 12 was complicated by an injury to the radial nerve and severe hemorrhage. A Kirschner wire was inserted through the olecranon from which a five-pound weight was suspended for the first 16 days.

TABLE I

SUMMARY OF FRACTURES OF THE UPPER THIRD OF THE HUMERUS INCLUDING THE SURGICAL NECK—  
IN GOOD OR FAIR POSITION

Case No.	Age	Sex	Type of Fracture	Date of Injury	Encase-ment Applied	Number of Weeks in En-casement	Final X-ray	Physio-therapy	Function of Shoulder
1. A. B.	70	F.	Oblique	1- 2-37	1- 2-37	7	Excellent	For 4 wks.	Excellent
2. E. S.	57	F.	Irregular, transverse	1-14-37	1-14-37	6	Excellent	No	Excellent
3. J. T.	67	F.	Oblique, comminuted	1-23-37	1-23-37	6	Good	No	Excellent
4. I. J.	70	F.	Irregular, oblique	2- 1-37	2-15-37	6	Good	No	Good
5. R. L.	45	M.	Oblique	2- 1-37	2- 1-37	4	Excellent	No	Excellent
6. A. B.	54	M.	Oblique	2- 5-37	2- 6-37	5	Excellent	No	Excellent
7. J. P.	44	M.	Transverse	2- 5-37	2- 5-37	6	Excellent	No	Excellent
8. H. C.	27	M.	Spiral, comminuted	2- 6-37	2-11-37	6	Excellent	No	Excellent
9. M. K.	16	F.	Transverse	2-13-37	2-16-37	5	Excellent	No	Excellent
10. L. C.	32	F.	Oblique	2-22-37	2-25-37	6	Excellent	No	Excellent
11. J. H.	10	M.	Irregular, transverse	3-13-37	3-13-37	5	Good	No	Excellent
12. C. K.	58	F.	Oblique, comminuted	4- 8-37	4-24-37	4	Good	No	Good
13. M. J.	45	F.	Oblique	4- 9-37	4- 9-37	7	Excellent	For 2 wks.	Excellent
14. V. M.	52	F.	Oblique, comminuted	5- 3-37	5- 3-37	6	Excellent	For 1 mo.	Good
15. D. B.	9	F.	Oblique	5- 6-37	5- 6-37	5	Excellent	No	Normal
16. M. O.	60	F.	Transverse	5-31-37	6- 1-37	7	Excellent	No	Excellent
17. V. H.	40	M.	Spiral, oblique	6-13-37	6-15-37	5	Good	No	Good
18. M. B.	68	M.	Transverse	7- 9-37	7- 9-37	4	Excellent	No	Excellent
19. A. M.	79	F.	Irregular, transverse	7-26-37	7-26-37	7	Fair	No	Good
20. R. R.	82	M.	Oblique	8-21-37	8-22-37	8	Excellent	No	Excellent
21. J. S.	7	M.	Transverse	9-15-37	9-15-37	5	Excellent	No	Normal
22. J. R.	60	M.	Oblique	9-22-37	9-22-37	7	Excellent	No	Excellent
23. A. J.	21	M.	Oblique, comminuted	2-27-38	3- 1-38	9	Excellent	No	Excellent
24. I. J.	60	M.	Irregular, transverse	4-19-37	4-19-37	6	Excellent	No	Excellent
25. H. C.	64	M.	Oblique	5-14-38	5-14-38	6	Excellent	No	Excellent
26. W. Y.	66	M.	Spiral, oblique	7-19-38	7-19-38	12	Excellent	No	Good
27. R. M.	15	F.	Oblique	8-10-38	8-10-38	4	Excellent	No	Normal
28. M. B.	47	F.	Oblique	10- 7-38	10- 7-38	8	Excellent	For 2 wks.	Excellent
29. G. S.	61	M.	Transverse	12- 5-38	12- 5-38	6	Excellent	No	Excellent
30. M. D.	53	M.	Oblique	12-24-38	12-24-38	6	Excellent	No	Excellent
31. L. R.	47	M.	Oblique	1-14-39	1-14-39	5	Good	No	Excellent
32. S. B.	68	F.	Oblique	2-17-39	2-17-39	5	Excellent	No	Excellent
33. M. R.	55	F.	Transverse	2-17-39	2-18-39	4	Excellent	For 2 wks.	Excellent
34. J. S.	67	M.	Irregular, oblique	3-18-39	3-24-39	5	Excellent	No	Excellent
35. J. L.	43	M.	Transverse, comminuted	3-19-39	3-19-39	7	Good	No	Fair
36. G. B.	13	M.	Epiphyseal separation	5-13-39	5-13-39	4	Excellent	No	Excellent
37. A. R.	8	M.	Transverse	5-27-39	5-27-39	5	Excellent	No	Excellent
38. C. M.	35	F.	Transverse, impacted	6-17-39	6-17-39	7	Excellent	No	Excellent
39. D. M.	15	M.	Oblique	6-24-39	6-24-39	6	Excellent	No	Excellent
40. F. K.	67	M.	Oblique, comminuted	7- 5-39	7- 5-39	10	Good	No	Good
41. M. P.	10	F.	Transverse	7- 8-39	7- 8-39	5	Excellent	No	Excellent
42. J. L.	70	M.	Oblique	7-25-39	7-26-39	6	Excellent	No	Excellent
43. L. S.	39	F.	Oblique, comminuted	8-26-39	8-29-39	7	Excellent	No	Excellent
44. M. W.	37	M.	Shattering	9- 3-39	9- 3-39	14	Excellent	No	Good
45. J. P.	31	M.	Oblique, comminuted	9-11-39	9-11-39	9	Excellent	No	Excellent
46. S. M.	15	M.	Oblique	9-26-39	9-26-39	5	Excellent	No	Excellent
47. W. H.	36	M.	Oblique	10-13-39	10-14-39	5	Excellent	No	Excellent
48. C. H.	11	F.	Oblique	12-13-39	12-13-39	6	Excellent	No	Excellent
49. D. E.	85	F.	Oblique	1- 6-40	1- 6-40	7	Excellent	No	Excellent

# FRACTURES OF THE HUMERUS

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TABLE II  
SUMMARY OF FRACTURES OF THE UPPER THIRD OF THE HUMERUS INCLUDING THE SURGICAL NECK—IN POOR POSITION

Case No.	Age	Sex	Date of Injury	Type of Displacement	Corrective Procedure	Number of Weeks in Encasement	Final X-ray	Physiotherapy	Function of Shoulder
50. J. Q.	61	M.	1-12-37	Shaft medial to head, with $\frac{1}{2}$ inch overriding	"Hanging cast" for 2 wks., then open reduction and shoulder spica; with arm in abduction for 3 wks.; "hanging cast"; "hanging cast"	7	Poor	For 2 wks.	Poor
51. I. S.	50	F.	2-4-37	Shaft displaced medialward $\frac{1}{2}$ inch overriding, lateral	Manipulation; "hanging cast"	7	Good	No	Excellent
52. A. T.	10	F.	3-1-37	Outward bowing, with $\frac{1}{4}$ inch overriding	"Hanging cast"	6	Excellent	No	Excellent
53. J. H.	51	M.	3-30-37	$\frac{1}{2}$ inch medial displacement of shaft	"Hanging cast"	8	Excellent	For 2 wks.	Excellent
54. B. S.	79	F.	4-2-37	$\frac{1}{4}$ inch overriding, shaft lateral to head	Manipulation; "hanging cast"	5	Excellent	No	Excellent
55. A. J.	66	M.	4-21-37	Lateral angulation, not in apposition	"Hanging cast"	5	Excellent	No	Excellent
56. H. W.	32	M.	6-2-37	Shaft medial to head	"Hanging cast"	6	Excellent	No	Excellent
57. K. O.	5	F.	7-8-37	Shaft lateral to head	"Hanging cast"	5	Excellent	No	Excellent
58. J. T.	45	M.	7-24-37	Shaft medial to head, $\frac{1}{4}$ inch overriding	"Hanging cast"	5	Excellent	No	Excellent
59. L. G.	12	M.	8-18-37	$\frac{1}{2}$ inch overriding, lateral separation	"Hanging cast"	5	Good	No	Excellent
60. M. L.	43	M.	10-16-37	$\frac{1}{2}$ inch overriding, lower fragment medial to upper	"Hanging cast"	5	Good	No	Excellent
61. W. F.	57	M.	1-1-38	Lateral apposition, rotation of head	Manipulation; "hanging cast"	6	Good	No	Good
62. F. W.	70	F.	4-5-38	Anterior and medial displacement of shaft; marked rotation of head	Skeletal traction for two weeks, then open reduction and 90° abduction in encasement for three weeks; "hanging cast"	3	Good	No	Fair
63. F. O.	42	M.	4-9-38	Marked lateral angulation and lateral separation	Manipulation; "hanging cast"	6	Good	No	Excellent
64. G. H.	75	M.	5-6-38	Shaft medial to head, head rotated	Manipulation; "hanging cast"	6	Fair	No	Good
65. C. L.	49	M.	7-24-38	Impacted, considerable lateral angulation	Manipulation; and "hanging cast" for two weeks, then skin traction following a second manipulation for two weeks, then "hanging cast"	6	Excellent	No	Excellent
66. L. B.	60	M.	4-2-39	$\frac{1}{2}$ inch overriding	Manipulation; "hanging cast"	7	Excellent	For 2 wks.	Excellent
67. B. P.	55	M.	3-23-39	Shaft medial to head	"Hanging cast"; "hanging cast" with sponge rubber pad in axilla	6	Excellent	No	Excellent
68. M. G.	29	M.	7-23-39	Shaft medial to head	"Hanging cast"; "hanging cast" with sponge rubber pad in axilla	6	Excellent	No	Excellent
69. M. D.	51	M.	11-1-39	Shaft medial to head	"Hanging cast"; "hanging cast" with sponge rubber pad in axilla	7	Excellent	No	Excellent
70. M. P.	34	F.	12-4-39	Shaft medial to head, $\frac{1}{2}$ inch overriding	"Hanging cast"; "hanging cast" with sponge rubber pad in axilla	6	Excellent	No	Excellent
71. F. F.	71	M.	1-12-40	Shaft displaced medially	"Hanging cast"; "hanging cast" with sponge rubber pad in axilla	8	Excellent	For 2 wks.	Excellent
72. I. W.	43	M.	1-24-40	Shaft displaced medially	"Hanging cast"; "hanging cast" with sponge rubber pad in axilla	7	Excellent	No	Excellent



FIG. 4.—Roentgenogram of a fracture of the surgical neck of the humerus before application of the hanging case.



FIG. 5.—Roentgenogram of the same patient shown in Figure 4, two days after the application of the hanging case.

Case 34 suffered from delirium tremens which necessitated restraining the patient in bed for eight days. During this time the fractured arm was strapped to his side.

Five of the 49 patients in Group 1 had compound fractures (Cases 8, 12, 23, 44 and 45). All were gunshot wounds except Case 12. Case 35 was a fracture through a bone cyst in the upper third of the shaft of the humerus. Healing of the fracture did not result in the disappearance of the cyst.

The length of time that the encasement was left on in this group ranged from 4 to 14 weeks, the average time being about six and one-half weeks. Union was prompt in all fractures except Case 44. This had a badly shattered fracture caused by a gunshot wound, which required 14 weeks before union became sufficient to permit removal of the encasement.

Excellent function of the shoulder was obtained in 40 cases. Eight patients obtained only  $90^\circ$  shoulder abduction. One patient (Case 35) was very uncoöperative from the beginning, and persistently removed the sling from his neck and carried the arm buttoned inside his shirt. When last seen, three months after removal of his encasement, he had only  $60^\circ$  shoulder abduction. This probably could have been improved by physiotherapy, but the patient refused treatment.

Table II summarizes the study of 23 fractures of the upper third of the humerus which were in poor position, as shown roentgenologically. The youngest age was age 10, and the oldest 76. In many the deformity was apparent on physical examination. In 11 cases the shaft was displaced



# FRACTURES OF THE HUMERUS

TABLE III  
SUMMARY OF FRACTURES OF THE MIDDLE AND LOWER THIRD OF THE HUMERUS—IN GOOD OR FAIR POSITION

Case No.	Age	Sex	Type of Fracture	Encasement		Number of Weeks in	Final X-ray	Physiotherapy For 2 wks.	Function of		Cosmetic Result
				Applied	Date of Injury				Elbow and	Shoulder	
73. R. B.	8	M.	Transverse, middle third	1-18-37	1-16-37	6	Excellent	No	Normal	Excellent	Excellent
74. J. M.	12	M.	Irregular transverse, middle third	4-27-37	4-20-37	7	Good	No	Excellent	Excellent	Excellent
75. K. S.	21	F.	Oblique comminuted, middle and lower third	5-18-37	5-17-37	8	Excellent	No	Normal	Normal	Excellent
76. A. N.	59	M.	Oblique, middle third	5-18-37	5-18-37	5	Excellent	No	Normal	Normal	Excellent
77. S. G.	30	M.	Oblique, middle third	6-22-37	6-20-37	5	Excellent	No	Normal	Normal	Excellent
78. A. W.	43	F.	Spiral, oblique, lower and middle third	6-21-37	6-20-37	6	Excellent	No	Normal	Normal	Excellent
79. A. C.	11	M.	Transverse, middle third	9-11-37	9-11-37	5	Excellent	No	Normal	Normal	Excellent
80. B. P.	28	F.	Irregular, oblique, middle third	9-25-37	9-21-37	5	Excellent	No	Normal	Normal	Excellent
81. M. T.	45	M.	Irregular, transverse, middle third	3-8-38	3-5-38	8	Excellent	No	Normal	Normal	Excellent
82. J. G.	45	M.	Oblique, lower and middle third	4-20-38	4-11-38	5	Excellent	No	Normal	Normal	Excellent
83. C. R.	47	M.	Oblique, lower and middle third, eight months old with nonunion	8-20-38	12-25-37	10	Excellent	No	Good	Good	Excellent
84. E. S.	15	M.	Transverse, middle third	10-25-38	10-11-38	5	Excellent	No	Excellent	Excellent	Excellent
85. R. C.	17	M.	Shattering (gunshot), lower and middle third	2-8-39	1-17-39	5	Excellent	For 6 wks.	Excellent	Excellent	Excellent
86. J. S.	28	F.	Irregular, transverse, middle third	2-8-39	2-7-39	7	Excellent	No	Excellent	Excellent	Excellent
87. E. T.	54	M.	Oblique, middle third	7-1-39	7-1-39	8	Excellent	No	Normal	Normal	Excellent
88. J. V.	66	M.	Oblique, middle third	12-15-39	12-15-39	6	Excellent	No	Normal	Normal	Excellent
89. A. F.	13	F.	Transverse, middle third	12-23-39	12-22-39	6	Excellent	No	Normal	Normal	Excellent
90. S. M.	40	M.	Oblique, middle third	1-27-40	1-27-40	5	Excellent	No	Normal	Normal	Excellent
91. A. A.	24	F.	Oblique, lower and middle third	2-16-40	2-16-40	6	Excellent	No	Normal	Normal	Excellent

medially to the head; four of these were overriding. Four had the shafts displaced laterally, while in two cases the humeral head was markedly rotated.

Thirteen patients had encasements applied without any previous attempt at reduction. In three of these cases, a sponge rubber roll, placed high in the axilla, corrected the medial displacement of the shaft. Seven were successfully reduced before application of the encasement by manipulation under fluoroscopic control. Two had general anesthesia, while one had a local anesthetic; four were seen early and were manipulated without anesthesia.

In Case 67, impaction was broken up, and lateral angulation corrected under general anesthesia. A check-up roentgenogram, taken two weeks later, showed the humeral shaft to be displaced medialward. The hanging plaster case was then removed, and the fracture reduced by a second manipulation under general anesthesia. Reduction was successfully maintained by skin traction to the upper arm, with the elbow flexed to 90°. Traction was discontinued after two weeks and a second encasement was applied.

In this group, exclusive of those fractures that were treated by open reduction or by traction before application of the encasement, an average period of six weeks was spent in the plaster case.

Excellent shoulder function was obtained in 18 cases. Three cases had limitation of shoulder abduction to 90°. Cases 50 and 64, which had open reductions, obtained 60° and 80° abduction, respectively. Physiotherapy for two weeks in Case 50 did not effect any improvement.

Table III summarizes the data of 19 patients who sustained fractures of the middle and lower thirds of the humerus, with little or no displacement. Their ages varied from eight to 66 years.

Plaster encasements were applied over a period ranging from a few hours to four days following injury, except in four cases (Cases 82, 83, 84, and 85). Manipulative and other corrective procedures were not necessary.

Delirium tremens in Case 82 caused a nine-day delay in application of the encasement. Case 83, when admitted to the hospital, had a delayed union of a fracture sustained approximately eight months previously. This patient, affected by a mental derangement, was deemed a poor operative risk. However, after ten weeks' treatment in a hanging plaster case union was solid.

Case 84 had a skull fracture in addition to the humeral fracture. He was placed in skin traction for 14 days, followed by the hanging plaster case.

Case 85 was a gunshot wound. After débridement and closure, skeletal traction through the olecranon was applied. After three weeks skeletal traction was discontinued and the arm treated with a hanging plaster case.

The average length of time of treatment with the hanging case in this group, exclusive of those in which there was delay of more than four days before application of the encasement, was approximately six weeks.

Uniformly, excellent functional and cosmetic results were obtained in this group. Only one patient had limitation of motion, and this fracture, as

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TABLE IV  
SUMMARY OF FRACTURES OF THE MIDDLE AND LOWER THIRD OF THE SHAFT OF THE HUMERUS—IN POOR POSITION

Case No.	Age	Sex	Date of Injury	Type of Fracture	Corrective Procedure	Number of Weeks in En-casement	Final X-ray	Physio-therapy	Function of Elbow and Shoulder	Cosmetic Result
92. L. B.	45	F.	1-23-37	Transverse, 1/2 inch overriding	Manipulation under general anes-thesia; "hanging cast"	9	Excellent	No	Excellent	Excellent
93. E. W.	50	F.	1-23-37	Transverse, 1/2 inch overriding, an-terior bowing, 1/2 inch overriding, marked anterior angulation	"Hanging cast"	5	Excellent	For 2 wks.	Normal	Excellent
94. G. W.	64	M.	3-3-37	Oblique, 1/2 inch overriding	"Hanging cast"	10	Good	For 2 wks.	Normal	Excellent
95. A. H.	14	F.	3-6-37	Oblique, 1/2 inch overriding	Manipulation without anesthesia; "hanging cast"	6	Excellent	No	Normal	Excellent
96. N. C.	44	M.	3-28-37	Oblique, 1/2 inch overriding	"Hanging cast"	6	Excellent	No	Normal	Excellent
97. A. K.	52	M.	5-27-37	Irregular, transverse, 1/2 inch over-riding	"Hanging cast"	9	Excellent	For 2 wks.	Excellent	Excellent
98. A. J.	43	M.	6-5-37	Oblique, comminuted, marked an-terior bowing	"Hanging cast"	10	Excellent	No	Good	Excellent
99. R. M.	10	M.	6-5-37	Transverse, 3/4 inch overriding, com-pound	"Hanging cast"	5	Excellent	No	Excellent	Excellent
100. S. M.	8	F.	6-15-37	Oblique, 1/2 inch overriding	"Hanging cast"	5	Excellent	No	Excellent	Excellent
101. A. D.	30	M.	7-2-37	Transverse, 1 1/2 inches overriding	"Hanging cast"	9	Good	For 2 wks.	Good	Excellent
102. F. L.	16	M.	7-27-37	Oblique, lateral separation of frag-ments	"Hanging cast"	7	Good	No	Good	Excellent
103. P. L.	13	M.	8-8-37	Oblique, anterior and lateral dis-placement of lower fragment	"Hanging cast"	5	Good	No	Excellent	Excellent
104. O. F.	33	M.	8-6-37	Transverse, 1/2 inch overriding	Manipulation; "hanging cast"	4	Good	No	Excellent	Excellent
105. A. C.	21	M.	12-2-37	Spiral oblique, 1/2 inch overriding	"Hanging cast"	7	Good	No	Normal	Excellent
106. S. K.	34	F.	2-5-38	Oblique, 1/2 inch overriding	Manipulation without anesthesia; "hanging cast"	7	Good	No	Excellent	Excellent
107. A. W.	82	F.	3-9-38	Spiral oblique, 1 inch overriding	"Hanging cast"	9	Good	No	Excellent	Excellent
108. P. M.	23	F.	3-27-38	Oblique, comminuted, 1 inch over-riding	Skin traction for 4 weeks; "hanging cast"	8	Good	No	Excellent	Excellent
109. W. C.	53	M.	5-8-38	Irregular, oblique, 1 inch overriding	Attempted reduction by manipula-tion under general anesthesia, skeletal traction for 2 weeks; "hanging cast"	5	Good	No	Excellent	Excellent
110. W. B.	13	M.	7-22-38	Oblique, 3/4 inch overriding	Skin traction for 1 week; "hanging cast"	8	Excellent	No	Normal	Excellent
111. M. G.	40	M.	7-20-38	Oblique, 1/2 inch overriding	"Hanging cast"	9	Good	No	Excellent	Excellent
112. R. M.	86	M.	8-12-38	Spiral, oblique, comminuted, lateral separation of fragments, anterior bowing	"Hanging cast"	7	Excellent	No	Excellent	Excellent
113. V. B.	22	M.	11-23-38	Oblique, comminuted, anterior bow-ing	"Hanging cast"	6	Excellent	No	Normal	Excellent
114. T. H.	32	M.	12-30-38	Oblique, 1 inch overriding	"Hanging cast"	8	Good	No	Normal	Excellent
115. H. S.	65	M.	1-13-39	Oblique, 1 inch overriding	Skeletal traction for 3 weeks; "hang-ing cast"	6	Excellent	No	Excellent	Excellent
116. G. R.	79	M.	5-3-39	Oblique, 1/2 inch overriding	"Hanging cast"	7	Excellent	No	Normal	Excellent
117. R. C.	22	M.	7-4-39	Oblique, comminuted, 1/2 inch over-riding	"Hanging cast"	6	Excellent	No	Normal	Excellent
118. L. E.	23	M.	10-20-39	Oblique, comminuted, 1 inch over-riding	"Hanging cast"	5	Excellent	No	Normal	Excellent
119. J. V.	38	M.	2-13-40	Oblique, lateral apposition, anterior bowing	"Hanging cast"	6	Excellent	No	Normal	Excellent



FIG. 8.—Roentgenogram of a fracture of the lower third of the humerus.

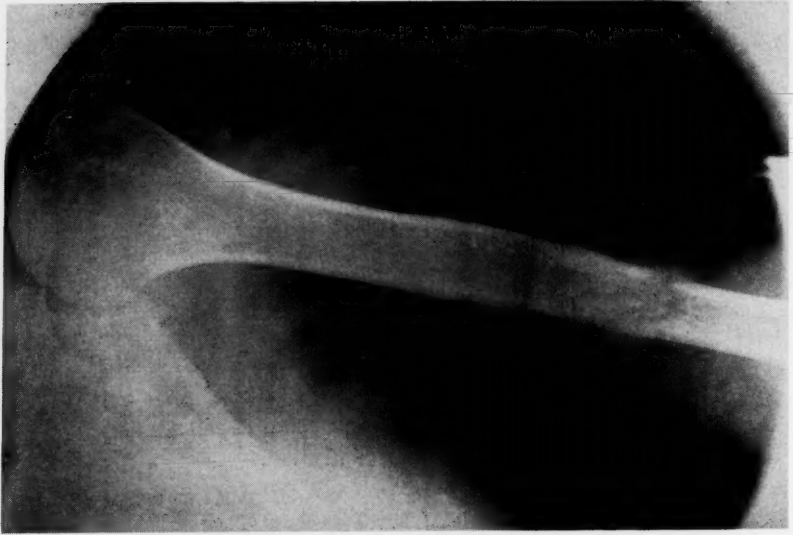


FIG. 7.—Roentgenogram of the same patient as shown in Figure 6, six weeks after the application of the hanging case.



FIG. 6.—Roentgenogram of a fracture of the middle third of the humerus.

previously reported, had been an eight-month delayed union before coming under observation. However, 90° active abduction and 75° external rotation had been obtained.

Table IV summarizes 27 fractures involving the middle and lower third of the shaft of the humerus in poor apposition and alignment, the patients ranging in age from eight to 86 years. Twenty-two of these fractures were overriding, three laterally separated, without overriding, and two were badly comminuted, with marked anterior bowing (Figs. 6, 7, 8 and 9).

In 19 instances no corrective procedures other than application of the hanging plaster case were used. Three others were successfully reduced by manipulation without the aid of anesthesia, while one required a general anesthetic. An attempted manipulation under general anesthesia resulted in failure in one instance. For two weeks, this patient was placed in skeletal traction



FIG. 9.—Roentgenogram of the same patient as shown in Figure 8, five weeks after application of the hanging case.

which brought the fragments into position and maintained them there. The remaining three patients were previously treated by traction; one by skeletal traction for three weeks, and the other two by skin traction for two and three weeks, respectively.

This group of patients required a slightly longer period in the encasement than the other three groups. The average length was approximately seven weeks.

The end-results for function of the shoulder in 25 cases were excellent. Two had only slight limitation of motion. Cosmetic results were excellent in all.

#### SUMMARY

(1) Since 1935, the majority of fractures of the neck and shaft of the humerus have been successfully treated on the Bone and Joint Service of Receiving Hospital by the hanging plaster case.

(2) A report of the final results obtained in 119 consecutive cases treated by the hanging plaster case is presented. This brings up to date the results of cases treated by this method in our department since a similar report was made, in 1937, of the first 58 cases treated here in this manner.



(3) For consistency in describing end-results, we have again, as in the first report, used the terms "excellent," "good," "fair," and "poor."

(4) Little change has been made in the essential details of this method of treatment since it was first begun. Indications for and exceptions of its use have remained the same.

(5) In several cases of this series, displaced fractures became reduced shortly after application of the encasement. Others were reduced before this was applied.

(6) In fractures of the neck, medial angulation is satisfactorily reduced in some patients by means of a sponge rubber roll placed high in the axilla.

(7) Lateral angulation in fractures of the shaft is corrected by a wedge on the inner side of the encasement at the elbow.

(8) Anterior and posterior angulation is corrected by shortening or lengthening the sling.

(9) Seventy-two fractures of the upper third of the humeral shaft and neck were all successfully treated by the hanging plaster case.

(10) Forty-seven fractures of the middle and lower thirds of the humeral shaft have been treated with satisfactory results.

(11) Early motion of the wrist and shoulder is encouraged. This prevents muscular atrophy and allows early return of maximum function.

(12) The hanging plaster case allows the patient to become ambulatory in a minimum length of time, without having the annoyance of cumbersome appliances necessary for treatment in the abducted position.

(13) The average length of time of treatment in the encasement, for all patients in this series, was approximately six weeks.

(14) The hanging plaster case is economical in that it reduces hospitalization time, dependent care, and the cost of materials used.

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## THE EARLY DIAGNOSIS OF POTT'S DISEASE\*

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SUCCESSFUL and satisfactory treatment of tuberculous lesions is dependent to a very considerable extent upon early diagnosis. This is as true for Pott's disease as it is for other lesions of tuberculosis. Yet it is common experience that most cases of Pott's disease pass through a long period in which the true nature of the disease is not recognized and diagnoses such as arthritis, myalgia, and sprain are made to explain the patient's symptoms. The true nature of the disease usually is not recognized until the vertebral bodies have undergone such destruction as to cause obvious deformity or until a frank abscess has manifested itself. By that time, the features of the disease in its advanced stages are so obvious that it can be recognized at a glance. Usually, it has taken three or more years to reach this stage. Yet, even in its early stages, Pott's disease presents diagnostic features by which it can be recognized. They are much less obvious than are the features of the later stages of the disease, and in some respects quite different. For that reason, it is worth while to draw attention to them.

Important information from which the early diagnosis of Pott's disease may be made is obtained from three sources: (1) The quality of the pain; (2) the roentgenogram; and (3) the recovery of tubercle bacilli from the lesion.

*Pain.*—This is the earliest symptom of Pott's disease, but for a variety of reasons it may not attract attention to the spinal focus. In the first place, the degree of pain often is surprisingly slight. Also, the onset may be so insidious and the progress so gradual that the patient is hardly able to tell when discomfort becomes pain. It is a common experience to have patients with Pott's disease admitted for treatment who have worked, sometimes at such strenuous occupations as farming, up to the moment of admission. The slight intensity of the pain and the fact that the patient is still working should not lead us to exclude Pott's disease. On the contrary, a pain which is persistent over a long period of time, even though it is of mild degree, demands investigation.

A feature of the pain associated with early Pott's disease, which can divert attention from the real source of the disease, is its reference to parts distant from the diseased segment of the spine. The pain of Pott's disease may manifest itself (1) in the back at the level of the disease (*i.e.*, local pain); or (2) in distant areas which are in spinal segments corresponding to the diseased areas (referred pain). Local pain and referred pain may both be present at the same time or one or the other may be present alone. The referred pain may be present on one side only or may occur on both sides.

\* Presented by title before the American Surgical Association, White Sulphur Springs, W. Va., April 28-30, 1941.

When Pott's disease manifests itself solely or chiefly by referred pain, it is not surprising that attention is diverted from the real source of the disease. Operations for appendicitis and even renal stone are not infrequent in the history of Pott's disease. Subsequent developments demonstrate that these were undertaken for pain referred from spinal disease.

The pain of Pott's disease, nevertheless, presents certain manifestations which should make it easy to recognize as being of spinal origin even though the referred element of the pain dominates the picture. In the first place, bilateral reference of the pain should always make one suspect its spinal origin. Pain on both sides of the trunk or in both legs can only mean (1) bilateral disease; or (2) bilateral reference of pain from a central origin in the spinal column or spinal cord. But the chief distinguishing features of the pain of Pott's disease arise from the fact that it is due to disease of the skeleton and hence is affected by activities in which the skeleton is involved. In any early case of Pott's disease, an inquiry into the factors which intensify the pain will quickly reveal that movements of the spine, increased weight-bearing by the spine (lifting, standing) and jolting of the spine (stepping down steps, riding in a car) all intensify the pain. Sometimes the activities which intensify the pain are so dramatic that they constitute manifestations of particular value. Thus, the explosive muscular efforts of coughing and sneezing cause great intensification of the pain, often spontaneously related by the patient.

Conversely, the pain of spinal disease is relieved by rest. The relief of weight-bearing which occurs when the patient is recumbent, especially if he lies prone and still, is as definite as is the intensification of the pain by movement, increased weight-bearing and jolting.

These aspects of the pain of Pott's disease enable us to recognize its spinal origin. They are not, however, specific for Pott's disease. Any spinal disease manifests itself by this type of pain. But one can, by these features, exclude disease in the area to which the pain is referred and localize the disease in the spine. Other manifestations enable us to recognize the disease as due to the tubercle bacillus.

*Roentgenologic Examination.*—The early radiographic changes in Pott's disease are quite distinctive and characteristic, though they differ greatly from those noted in the later stages of the disease. Little has been said or written regarding these early roentgenographic changes, and because of this the diagnosis of the disease often is postponed until the more familiar radiographic changes of the advanced stages have developed.

The earliest roentgenographic change in Pott's disease is thinning of an intervertebral disk, with or without evidences of destruction of the surfaces of the two adjacent bodies which bound the involved disk. On the evidence of the roentgenogram, one is justified in believing that the primary lesion of Pott's disease starts on the inferior or superior surface of a vertebral body, rapidly destroys the intervertebral disk and spreads across it to the adjacent surface of the vertebral body next above it or below. Then follows more or less extensive destruction of the two involved bodies with spread up and down

to other bodies. The very earliest change which is detectable is thinning of the intervertebral disk, and commonly at this stage the carious changes in the vertebral bodies are so slight as to be impossible of detection roentgenologically. It is a characteristic of Pott's disease, however, that the changes in the spine revealed roentgenologically are progressive, so that a series of roent-



FIG. 1A.

FIG. 1B.

FIG. 1.—Illustrates the value of a thin intervertebral disk as early evidence of Pott's disease.

Female, age 31, in June, 1938, commenced to experience pain in back radiating to leg. In July, a lumbar abscess formed. It contained tubercle bacilli. Figure 1A is the lateral radiograph, taken in September, 1938. It shows only a thin disk between L.V. 2 and 3. Figure 1B, taken in September, 1939 shows progress of the disease in one year—destruction of the intervertebral disk; and caries of the body of the 3rd lumbar vertebra. In September, 1938, the diagnosis of Pott's disease was confirmed by aspiration, and the recovery of tubercle bacilli in the pus obtained.

genograms, taken at intervals of a few months, reveal first a thin disk; then a thinner disk, with caries of the adjacent surfaces of the adjacent vertebral bodies; finally complete disappearance of the intervertebral disk, advanced caries, and collapse of the vertebral bodies. In the early stages of Pott's disease, the combination of pain, spinal in type, with the appearance of a thin disk in the roentgenogram, is of great significance.

The recovery of tubercle bacilli from a focus of Pott's disease or from the abscess associated with it, is indisputable evidence of the nature of the disease. In the later stages of the disease, this is easy, since an abscess of some sort is commonly present at that stage. It is not so generally known that important information can be obtained by deliberate aspiration of the spinal focus nor is the test commonly practiced. Under roentgenographic guidance it is possible, and not unduly difficult, to pass a long needle into the area of disease. The aspiration of even a small quantity of pus permits accurate diagnosis of the nature of the infection. Occasionally, organisms other than the tubercle bacillus produce spinal lesions indistinguishable by symptoms and

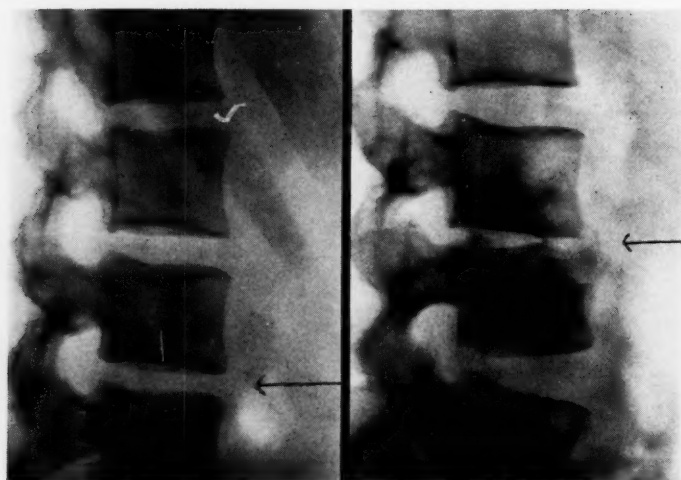


FIG. 2A.

FIG. 2B.

FIG. 2.—Illustrates the value of a thin intervertebral disk as early evidence of Pott's disease.

Female, age 19, while under treatment for tuberculosis of lung and ankle, complained of low back pain, radiating to right hip. Figure 2A, taken then, September, 1938, showed only a thin disk between L.V. 3 and 4. Figure 2B, taken in July, 1940, shows the progress of the disease, which now presents the characteristic roentgenographic appearance of Pott's disease.

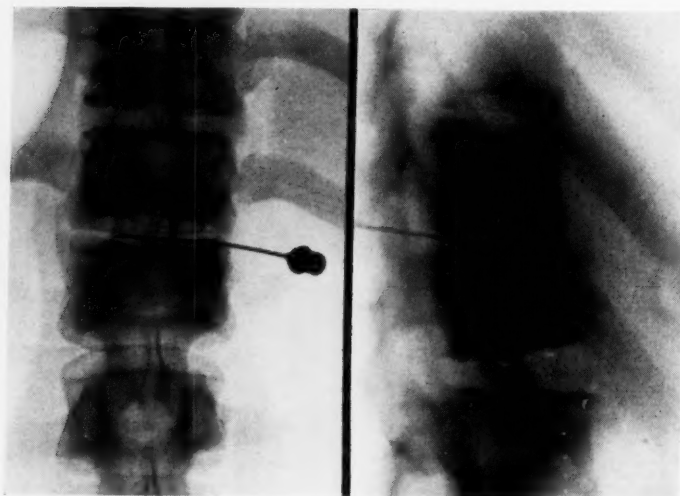


FIG. 3A.

FIG. 3B.

FIG. 3.—Illustrates the value of aspiration in the early and accurate diagnosis of Pott's disease, and of lesions resembling Pott's disease.

Male, age 19. In July, 1939, commenced to experience stiffness and aching in back, with pain which was accentuated by activity and relieved by rest. Figure 3A and B, in September, 1939, shows a thin disk between L.V. 12 and L.V. 1, and minimal caries of the anterosuperior corner of the body of L.V. 1. Radiologically, the picture is indistinguishable from early Pott's disease. The tuberculin skin test, however, was negative. Aspiration of the lesion, as illustrated, yielded a small amount of pus which grew staphylococci. *Diagnosis:* Staphylococcal osteomyelitis of spine. The course of the disease was satisfactory—early subsidence of the infection, with bony fusion of the involved vertebral bodies.



## POTT'S DISEASE

roentgenographic findings from Pott's disease. Aspiration of such foci gives early and accurate information of the nature of the infection.

### CONCLUSIONS

The diagnosis of Pott's disease in its earliest stages is a more difficult problem than is the recognition of the disease when well-established. It is important to make the diagnosis as early as possible in order that early treatment may enhance the prospect of cure. Certain of the early manifestations of the disease should be emphasized since their recognition permits early diagnosis.

Pott's disease may be diagnosed in its early stages by three important symptoms and signs:

- (1) Analysis of the pain from which the patient suffers demonstrates that it is of spinal origin (intensification by movement, weight-bearing and jolting; relief by rest).
- (2) The early roentgenographic evidence of a thin intervertebral disk before the characteristic caries of the vertebral bodies is manifest.
- (3) Aspiration of the focus under roentgenographic guidance yields pus from which a positive diagnosis can be made.

## "UNEXPLAINED" INFECTIONS IN CLEAN OPERATIVE WOUNDS\*

THE IMPORTANCE OF THE AIR AS A MEDIUM FOR THE TRANSMISSION OF PATHOGENIC BACTERIA; AND BACTERICIDAL RADIATION AS A METHOD OF CONTROL

ANALYSIS OF OVER FIVE THOUSAND OPERATIONS, COVERING A PERIOD OF TEN AND ONE-HALF YEARS

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AFTER ten and one-half years of intensive work in an attempt to avoid the operating room infections hitherto frequently referred to as "unexplained," it seems desirable to evaluate the results that have been obtained. Our experience can be divided roughly into three periods (Chart 1):

- (1) Before the institution of bactericidal radiation in the operating room on January 15, 1936—a period of five and one-half years—during which time infections continued to occur despite an increasing knowledge as to their cause and many efforts to eliminate them.
- (2) The transition years of 1936 and 1937, during which an increasing number of the staff adopted radiation as part of their "aseptic technic" for an ever-increasing number of their clean operations.
- (3) The years 1938–1941,† during which most of the large, clean operations have been performed in a field of sterile air, and infection in any clean primary incision has been extremely rare.

For the individual doctor or service, however, the simpler division is into operations performed *without* and the operations performed *with* bactericidal radiation. Regardless of what other measures, in addition to the usually accepted "aseptic and atraumatic technic," have been employed, before or since the introduction of radiation, in an effort to control these infections, the deciding factor in the improvements obtained seems to have been air sterilization.

The results obtained in various types of *large, clean operations* with and without the use of radiation, are summarized in Chart 2. Here it is seen that of a total of 1,735 such operations performed without radiation 207, or 11.9 per cent, showed infected wounds. Of these, 19 died as a result of their

\* Presented by title before the American Surgical Association, White Sulphur Springs, W. Va., April 28–30, 1941.

† The study was continued to January 15, 1941, in order to give five years' experience with bactericidal radiation, but the operations for the 14 days in January, 1941 are included in the 1940 column on each chart.

## INFECTED OPERATIVE WOUNDS

infection. On the other hand, of 2,463 similar operations performed under bactericidal radiation, wound infection developed in only six, or 0.24 per cent. None of the latter group of infections resulted in a fatality.

In the groups of operations reported (Charts 2-10 and Table I), both with and without radiation, all cases not potentially infected are included.

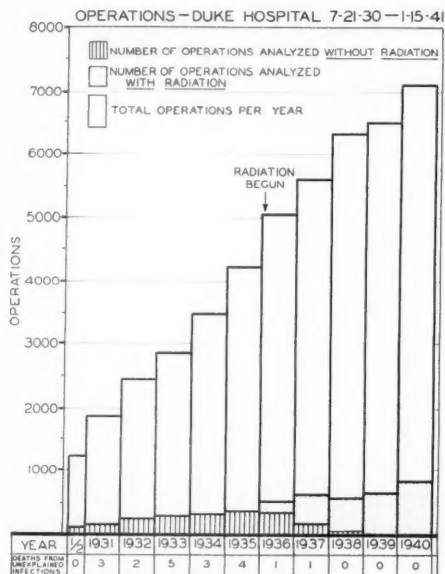


CHART 1.—This chart shows in addition to the growth of the Surgical Service of the Duke Hospital for the first ten and one-half years:

- (1) The small number of the total operations falling within the groups of large clean procedures (4,585\* out of a total of 46,369 [Charts 2-10 and Table I]) which have given us trouble from unexplained infections.
- (2) The distribution by years of all large clean operations which were analyzed in this study (see also Charts 4-10).
- (3) The ratio of the operations used for this analysis (i.e., the larger clean procedures) to the total operations performed, approximately 10 per cent, which represents the minimum number in the Duke Hospital which we feel should be performed in a field of sterile air.
- (4) The transition period—1936 and 1937—during which an increasing percentage of the larger clean operative procedures were performed in a field of radiation (see Charts 4-10).
- (5) The period from 1938 to 1941, during which practically all the large operations of the types indicated (Charts 2 through 10) were performed in a field of sterile air.
- (6) The distribution by years of the 19 deaths from "unexplained" infections all of which occurred in the relatively small group of operations (1,782) performed without radiation that were analyzed (see also Chart 3). In the comparable but considerably larger group of clean operations performed (2,600+)—including 140 reopened thoracoplasty wounds—with radiation, there was no death from an infected wound. Any deaths from an infected wound in the remainder of the operations (41,784) had a potential source of infection from the nature of the disease or operation.†

\* In addition to these operations, all of which are tabulated on Charts 2, and 4 through 10, the records of all deaths following operation, and not included in these groups (approximately 600), were reviewed to determine the number of patients who died of an unexplained infection in a clean wound (Chart 3).

† Just as in the large clean operations, these other operations, whether small and clean, grossly contaminated, or potentially infected, should have bacterial contamination kept to the minimum, and the tissues should be left in the best possible condition for healing. However, this subject will not be considered here, since it is not the problem with which we are dealing in this presentation.

The charts give a more detailed analysis of the different types of operations by years, the deaths that have occurred as a result of infections in clean wounds, the organisms that have caused the infections, and the improvement that has been obtained, predominantly by air sterilization.

Occasionally, the criticism has been made that the good results which we claim to have been obtained by air sterilization (Charts 2-10 and Table I) have been brought about by other improvements in technic. Many others who do not make this criticism at least raise this question. The answer is that for five years, and particularly after the disastrous three months in

PERCENTAGES OF INFECTIONS AND DEATHS FROM INFECTIONS IN 4,196 CLEAN OPERATIONS AND 187 REOPENED WOUNDS 7-21-30 — 1-15-41

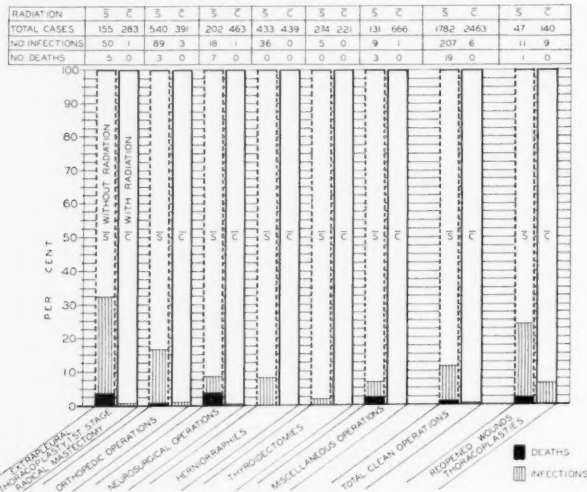


CHART 2.—This chart shows, in summary, for comparison, the results obtained without and with radiation in several types of clean primary operative procedures and in a group of reopened thoracoplasty wounds. The latter group of cases are recorded separately since they present a risk of infection as described under second and subsequent stage thoracoplasty (Chart 5) which is not present in clean primary incision. At the top are given the actual number of cases, the number of infections, and the number of deaths from infections for each group, while immediately below in the chart these figures have been transposed into percentages, for more accurate comparison of the results obtained without and with radiation in each type of operation. Deaths from "unexplained" infections have been eliminated when bactericidal radiation was used.

1933-1934 (Chart 3), we tried every improvement in technic that seemed feasible and to offer any hope of success, but without notable results, until the air-borne pathogenic bacteria (probably given off from the respiratory passages of the occupants of the operating rooms) were largely eliminated by ultraviolet radiation. Since this source of contamination (which we consider to overshadow all others where good technic, as we know it to-day, is used) has been largely eliminated, most of these previously adopted additions to technic, conceived in desperation and of questionable value, have been discarded.

For the information of those who feel that the improvement in our results was brought about by changes in technic other than air sterilization, these changes and additional precautions taken by us before beginning air sterilization in an effort to control these infections were given in a chronologic order but had to be eliminated from this publication because of its length. It will be seen, however, from an analysis of the charts, that the virtual elimination of operating room infections on different surgical divisions varied

# INFECTED OPERATIVE WOUNDS

## INFECTIONS IN CLEAN WOUNDS CAUSING DEATH

(7-21-30 TO 1-15-41)

1931	MARCH 21 MARCH 27	EXPLORATORY LAPAROTOMY CRANIOTOMY	PERITONITIS MENINGITIS	HEMOLYTIC STREPTOCOCCUS, STAPH. AUREUS STAPHYLOCOCCUS ALBUS
	DECEMBER 22	CEREBELLAR	MENINGITIS	STAPHYLOCOCCUS ALBUS
	FEBRUARY 2	ARTHROPLASTY HIP	SEPTICEMIA	BETA HEMOLYTIC STREPTOCOCCUS B. COLI COMMUNIOR
1932	NOVEMBER 1	SECTION 5TH NERVE	MENINGITIS	SMEAR-GRAM POSITIVE COCCI IN CLUMPS
	JANUARY 12	SPLENECTOMY	PERITONITIS	STAPHYLOCOCCUS AUREUS
1933	NOVEMBER 15 DECEMBER 6 DECEMBER 22 DECEMBER 26 JANUARY 16 JANUARY 26	THORACOPLASTY 1ST STAGE THORACOPLASTY 1ST STAGE OSTEOTOMY FEMUR THORACOPLASTY 2ND STAGE RADICAL MASTECTOMY SECTION 5TH NERVE	PULMONARY EMBOLI SEPTICEMIA EXTENSIVE INVASION NO BLOOD CULTURE SEPTICEMIA MENINGITIS	HEMOLYTIC STAPHYLOCOCCUS AUREUS HEMOLYTIC STAPHYLOCOCCUS AUREUS BETA HEMOLYTIC STREPTOCOCCUS, STAPH. AUREUS STAPHYLOCOCCUS AUREUS HEMOLYTIC STAPHYLOCOCCUS AUREUS HEMOLYTIC STAPHYLOCOCCUS AUREUS
1934	OCTOBER 31	SECTION 5TH NERVE	MENINGITIS	HEMOLYTIC STAPHYLOCOCCUS AUREUS
	APRIL 17	THORACOPLASTY 1ST STAGE	CHILL-- NO BLOOD CULTURE	HEMOLYTIC STAPHYLOCOCCUS AUREUS
1935	SEPTEMBER 16 OCTOBER 15 OCTOBER 27	CEREBELLAR THORACOPLASTY 1ST STAGE FUSION KNEE JOINT	MENINGITIS SEPTICEMIA SEPTICEMIA	GRAM POSITIVE DIPLOCOCCUS HEMOLYTIC STAPHYLOCOCCUS AUREUS BETA HEMOLYTIC STREPTOCOCCUS, STAPH. AUREUS
	APRIL 20	CRANIOTOMY **	MENINGITIS	STAPHYLOCOCCUS AUREUS--HEM. & NON-HEM.
1936				
1937				
	DECEMBER 9	EXCISION TUMOR NECK **	NO BLOOD CULTURE	HEMOLYTIC STAPHYLOCOCCUS AUREUS
1938 1939 1940				

\* FIRST RADIATION UNIT IN OPERATING ROOM INSTALLED 1-15-36

\*\* RADIATION NOT USED

CHART 3.—The fatalities from infection in clean wounds occurred only following operations where radiation was not used and were largely confined to neurosurgical, thoracic, and orthopedic operations. The four exceptions were two debilitated patients having celiotomies (inoperable carcinoma of the stomach, and cirrhosis of the liver with ascites), one woman of 73 having a radical mastectomy, and one man of 67 having an excision of a malignant tumor of the neck by a surgeon who was not accustomed to such a procedure.

The 19 fatal infections all occurred during the cooler months of the year during which time, in general, the air contamination is highest. Eleven, or 58 per cent,† became infected during November, December, January, and February; five, or 26.3 per cent, during October and March; and three, or 15.7 per cent, during September and April. There was no death from such an infection during May, June, July and August. In this chart each monthly division is blacked-out if one or more deaths occurred during the month. Note the proximity of the "black months" to the heavy lines dividing the chart into years.

Particular attention is also called to the disastrous three months of November, December, and January, 1933-1934, during which time there were six deaths from "unexplained" infections in clean wounds. Thus, over a period of ten and one-half years 31.6 per cent of all the deaths from "unexplained" infections occurred during a three-month period in a consecutive group of only 1.5 per cent of the total number of patients operated upon. A similar "epidemic" of operating room infections seemed to be under way in September and October, 1935, but was halted by discontinuing performing large operations that were not emergencies. At this time all patients in the hospital for extrapleural thoracoplasty were sent back to the sanatorium to await the months of lower air contamination or the completion of the preliminary experiments with, and the installation of adequate radiation equipment in the operating rooms.

There have been only two deaths from "unexplained" infections since the first radiation unit was installed, and in neither of these was it used. The left craniotomy, April 20, 1936, for what was considered before and found at operation to be an inoperable glioma, was performed without radiation since the only room equipped for radiation was in use for a laminectomy for removal of a benign spinal cord tumor.

The excision of the tumor of the neck, December 9, 1937, was performed by a surgeon who had never used bactericidal radiation, and who was inexperienced in neck surgery. The subsequent infection, caused by the hemolytic *Staphylococcus aureus*, spread extensively along the fascial planes, causing the patient's death. No blood culture was taken.

† This percentage is all the more impressive when consideration is given to the fact that after the epidemic of infections in November, December, and January, 1933-1934, large clean operations of election were postponed until the months of low air contamination, and for operations that could not be postponed until the summer, an attempt was made to anticipate and avoid the periods of greatest danger by daily cultures of the air in the operating rooms (References 3 and 12).



as to time, but in each it was simultaneous with the adoption of air sterilization. The improvement in results beginning with the institution of radiation has persisted despite the abandonment of many of the previously adopted precautions.

Undoubtedly, since 1936, there has been some improvement in wound healing as a result of our return to the use of silk in certain wounds, and as a result of the discontinuance of drainage in others. This is not the explanation of the virtual elimination of wound infections, however, as is illustrated by the fact that we were "brought-up" on silk technic, abandoned it temporarily only because of the prevalence of "unexplained" infections, and began using it again only after these "unexplained" infections had been explained and virtually eliminated by the use of ultraviolet radiation. Drainage of thoracoplasty wounds was begun as a result of frequent infections and was discontinued following the institution of radiation, but only after great improvement in wound healing had been obtained and after the drains in a number of cases had been cultured and no growth had been obtained. Catgut as a suture material is still used for all thoracoplasties, and there has been no change in the suture material used for neurologic and thyroid surgery (silk), and orthopedic surgery (catgut). During the past two years we have discontinued drainage of radical mastectomy wounds when radiation is used and find that, as a rule, they do not fill up with lymph, serum, or blood.

Previous publications on radiation have detailed:

- (1) The bactericidal and fungicidal effect of this radiation.<sup>2</sup>
- (2) The effect of radiation on wound healing.<sup>3, 4</sup>
- (3) The reduction in the number of wound infections in small series of operations.<sup>5, 6, 7</sup>
- (4) The reduction in the postoperative temperature reaction.<sup>8</sup>
- (5) The rôle of the respiratory tract in contamination of the air.<sup>13</sup>

The present report, covering a period of ten and one-half years, can be divided roughly into two parts: (I) An analysis of all deaths from infection following a clean operation\* during the time covered; and (II) an analysis of 1,313 selected clean operations (but including 47 reopened thoracoplasty wounds) before radiation was instituted, January 15, 1936; 469 similar clean operations performed without radiation after January 15, 1936; and all operations—2,803—(including 140 reopened thoracoplasty wounds [Chart 5] and something less than 200 potentially infected operative wounds, the latter included in the 866 miscellaneous operations [Chart 10]) performed with bactericidal radiation from January 15, 1936 to January 15, 1941.

#### (I) DEATHS

From July 21, 1930 to January 15, 1936 (when bactericidal radiation was first instituted), 15,674 operations of all types (Chart 1) were performed

\* Exclusive of Obstetrics and Gynecology, which is a separate service.

with 16 deaths from infections in clean primary incisions, and one death from infection in a clean reopened thoracoplasty wound. In contrast to this, during the five-year period, from January 15, 1936 to January 15, 1941, with a total of 30,695 operations (Chart 1) there have been *only two deaths* from infections in clean incisions, either primary or reopened, and both of these infections occurred in wounds that were not protected during operation by bactericidal radiation (Chart 3).

Particular attention is called to the fact, as shown in Chart 3, that each of the 19 patients who died from an infection in a clean incision had had a large operative procedure of a specialized type, with the exception of two debilitated patients who had a celiotomy which was followed by peritonitis.

Since deaths from infections in "clean wounds," where radiation is not used, are relatively rare and occur almost entirely in a few types of the larger procedures or in debilitated patients (Chart 3), they will be seen only rarely by the average surgeon. For them the elimination of the somewhat more frequent nonfatal infections and the improved healing in all wounds, even where the contamination does not go on to gross suppuration,\* probably results in a greater sum total of good than the saving of an occasional patient from the very rare fatal infection.

#### (II) INFECTIONS

All operations of several types† (Charts 1-10 and Table I) performed during a period of ten and one-half years have been reviewed. The post-operative notes and the temperature chart of every record have been reviewed in order to pick up any infections that may not have been included in the index file of postoperative infections. This was particularly important for the orthopedic operations, where the wound was under an encasement which frequently was not removed and the infection not diagnosed until a return visit to the Out-Patient Dispensary,‡ at which time the hospital record had been completed and indexed.

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\* The improvement in wound healing and the diminished systemic temperature reaction, both elevation and duration, brought about by radiation has been reported for small groups of cases (extrapleural thoracoplasties, radical mastectomies, and herniorrhaphies). These results, as given in a previous report,<sup>8</sup> were so conclusive, and such an analysis is so laborious and time-consuming, that it did not seem to be necessary or desirable to carry it out here with such a large series. The surgical staff, from clinical observation, are of the opinion that this average of diminished systemic temperature reaction as reported has been maintained throughout the entire series of operations where bactericidal radiation has been used.

† With the exception of an occasional record that could not be located.

‡ Some of these patients had their follow-up treatment in various Orthopedic Clinics over the state, so that our follow-up records were not complete. As a result, some mild or moderate infections, particularly where radiation was not used, undoubtedly have been missed.

Stitch abscesses were omitted\* for the entire group both with and without radiation since they are considered to be the reaction to a foreign body. They are particularly likely to develop when the suture is left in for too long a time, with the growth of the skin organisms already present. In no respect can they be considered as operating room infections, except on the very unlikely possibility that the sutures themselves were unsterile.

Unexplained operating room infections, particularly those of a serious nature, occur in only a small percentage of the general run of operations performed by well trained surgeons with a relatively good "atraumatic technic." However, during and following certain of the larger procedures, such as many of those included in this analysis, large areas of tissue are exposed for a long time, excessive trauma may be unavoidable, hemostasis may be difficult to obtain, dead space may not be obliterated, the patient may be in a debilitated condition or the tissues may offer little resistance to infection, cleavage planes or spaces may be opened for the relatively unimpeded spread of infection, immobility in the wound may be unobtainable, or packs or drains may have to be inserted, thus making it more likely that the organisms gaining access to the wound can cause an infection.

Furthermore, it is well known that at certain times the danger of "unexplained" infection in clean operative wounds is far greater than the average (Chart 3). Such a peak of danger with us is well illustrated in Chart 3, where it is seen that for the past ten and one-half years, since the opening of the Duke Hospital, 31.6 per cent of all the deaths (six patients) from "unexplained" operating room infections in clean wounds occurred during the three consecutive months of November, December, and January of the academic year 1933-1934. The total number of operations performed during these

\* In previous publications, the cases which we did not consider to have an operating room infection but which had a positive culture report on the record, were included with the abstracted infected cases, and the decision as to the true nature, origin, and severity of the condition was left to the reader. Such a policy could not be followed in this larger analysis since the results are presented in the form of charts. In order that the reader may make his own decision in these cases, reference is given to those previously published abstracts of operations which are omitted from the charts in this report since we do not consider them to have had "unexplained" operating room infections.

Abstracts in Reference 7:

Cases.—(1) Inguinal hernia—stitch abscess; (2) cerebellar exploration—stitch abscess; (3) laminectomy, fractured spine—contused wound with skin abrasions preoperative, but infection considered to be hematogenous; (4) arthroplasty hip—postoperative hemorrhage, drains left in wound; and (5) open reduction fracture-dislocation ankle—skin slough with superficial infection limited to area of slough.

Abstracts in Reference 9:

Cases.—(1) Inguinal herniorrhaphy—skin inversion only; (2) radical mastectomy—stitch abscess; (3) extrapleural thoracoplasty through scar—stitch abscess, maceration suture line; (4) extrapleural thoracoplasty, second stage—stitch abscess; (5) extrapleural thoracoplasty, first stage—pustular eruption (operative site before operation, delayed healing of skin incision, made with cutting electric current); and (6) extrapleural thoracoplasty, second stage (same patient as [5])—draining hematoma.

three months was only 708, or 1.5 per cent of the total of 46,369, for the ten and one-half-year period (Chart 1).

In analyzing these statistics on infections (Charts 1-10 and Table I) one should keep in mind that many of the operations reported (both with and without radiation) were the larger procedures, and, therefore, the ones most likely to become infected. (Ref. Chart 1 for percentage of total operations included in these groups.)

The operating room infections both with and without radiation have been classified as mild, moderate, severe, and as having caused the death of the patient.

(1) The mild infections were trivial, with little local or systemic reaction, and the minimum amount of pus.

(2) Those classed as moderate produced more systemic and local reaction and contained more pus than the mild group.

(3) Every infection with extensive involvement of the wound or a severe local or systemic reaction which did not kill the patient, was classed as severe, regardless of whether or not the life of the patient was threatened.

(4) Those classified as deaths from infection are self-evident. They are also listed separately in Chart 3, and have occurred only when bactericidal radiation was not used and following an extensive operation or an operation upon a debilitated patient.

The operations of each type covered by this survey can be divided roughly into three groups:

(1) All those performed during the first five and one-half years before bactericidal radiation was instituted. In this series the infection rate was highest, and the infections of greatest severity despite the many things that were tried in an effort to prevent them.

(2) All operations of the types analyzed, and performed without bactericidal radiation during the transition period from January 15, 1936 through 1938. In general, during this period (Charts 4-10 and Table I) the percentage of infections in operations where radiation was not used was lower, and when they occurred they were much less severe than in the previous years. This is explained by the fact that any service or any individual at first performed only the larger operative procedures, and, therefore, the ones most likely to become infected, in a field of bactericidal radiation, thus eliminating them from the nonradiated group. As the good results obtained in these larger operations became evident, an increasing percentage of the operations of less magnitude was also performed in a field of sterile air.

Operations performed without radiation after 1938 are not included in the charts since they were so few in number, usually small in size and frequently performed during the summer months when the air contamination was low, so an analysis would give no true idea of the risk of infection in the general run of such operations.

(3) In this group are all operations performed in a field of bactericidal

radiation after beginning its use for operations upon patients, January 15, 1936 (in general, the operations of greatest magnitude for any service or any individual during the period of transition, 1936-1938). Originally, sterilization of the air in the operating room by ultraviolet radiation was used only during extrapleural thoracoplasties, and no such operation has been performed without it since the first radiation unit was installed (Charts 4 and 5). Radical mastectomies were soon brought into the radiation group. The orthopedists gradually began using it for their larger operations in 1937 (Chart 6). The neurosurgeons began using it during 1936 (Chart 7) but temporarily abandoned it in the fall and winter of 1937-1938, for reasons explained in the text for Chart 7. Early in 1938, after the occurrence of a number of infections, it was resumed by this service for all except small procedures such as trephines, and infected cases which had to be drained (Chart 7).

Thyroids and herniae, because of their lesser magnitude, and because of the shortage of suitably equipped operating rooms, were only gradually brought into the radiation group (Charts 8 and 9). Radiation was used first in these operations, predominantly, for the larger operations and during the winter months when the air contamination was high, but later, in an increasingly high percentage of cases, throughout the entire years.\*

Since early in 1936, an increasing number of miscellaneous operations, a fair percentage of which were potentially infected, have been operated upon with radiation. These are all grouped together in Chart 10.

Charts 4-10, inclusive, show the incidence of infection in these various operative groups by years, with and without bactericidal radiation. In each group, a striking reduction in the frequency of wound infection occurred when radiation was used. In first stage thoracoplasties and radical mastectomies the infection rate dropped from 32 to 0.35 per cent; in orthopedic operations from 16.5 to 0.74 per cent; in neurosurgical operations from 9 to 0.22 per cent; in herniorrhaphies from 8.3 to zero per cent; and in thyroidectomies from 1.8 to zero per cent.

The criticism can be made justly that the experiment would have been more accurately controlled had alternate operations in each group been performed with and without radiation. However, by the time the radiation technic had been worked out, 17 patients had died as a result of an infection which we now consider to be largely preventable (Chart 3). Many others had had a needlessly prolonged convalescence and impairment of their operative results, while still others, because of the danger of infection at times of high air contamination, had been refused the advantages offered by operation. It did not seem to us justifiable, for the sake of the experiment, to subject any of these patients to a risk, which we were reluctant to take before bactericidal radiation was available.

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\* Radiation was started by one of us as an experimental project, to determine the effect of the elimination of air-borne bacteria during the operation on wound healing. Since that time all members of the surgical staff (General, Neurologic, Orthopedic, Plastic, Thoracic and Urologic) have, at their own request, adopted it as routine for their large clean operations.



The effect of this "fear of infection" on the growth of the Thoracic and Neurosurgical Services during 1933, 1934, and 1935, is illustrated in Charts 4, 5 and 7. In contrast to the continued growth of the entire service (Chart 1) the number of these operations per year remained at a standstill or actually diminished from 1933 through 1935, because of the hesitancy of the staff, except in emergency, to advise these large operations during certain times of the year when the air contamination was high.

A notable example of the effect of these infections and deaths on our method of treatment of patients, is the fact that after the fatalities from meningitis following section of the fifth nerve (Chart 3) most of these patients were treated by alcohol injection. Only after radiation had been instituted and proved to be an effective means of protecting these open wounds, did we resume section of the nerve by open operation. Beginning in 1936, the full year was made available for these more extensive operations by air sterilization, and immediately there was a great increase in the number of such operations performed (Chart 7).

#### THORACOPLASTY, FIRST STAGE, AND RADICAL MASTECTOMY—CHART 4

These two types of operation are combined to conserve space. Both involve wide exposure of tissues and, in our hands, had a high infection rate (25–38 per cent<sup>5, 6, 9</sup>), but with the more serious infections and the greater number of fatalities from infection in the thoracoplasty group (Chart 3). Otherwise, they are radically different in that the thoracoplasties are associated with more trauma, hemostasis is less satisfactory, there is residual dead space which cannot be obliterated, and there is more motion in the wound during the convalescent period. Before radiation was instituted, catgut was used for both, but since 1936 most of the mastectomies have been performed with silk while catgut is still used for the thoracoplasties. The unfavorable conditions for healing of the mastectomy wounds are the poor blood supply to the skin flaps, the tension which is at times present, and the occasional accumulation of lymph or blood beneath the flaps.

The diminishing number of operations each year, for 1933, 1934, and 1935, was a direct result of our refusal to operate upon patients for thoracoplasties during the winter months and the limited bed facilities during the summer. The two fatalities from infection in thoracoplasty wounds during 1935 occurred in April and October (Chart 3), at the beginning and end of what, at that time, we considered to be the best season for operating upon these patients. Because of the large number of patients needing this operation we had started "crowding the season" by admitting these patients in March and continuing to perform these operations in the fall. However, after the fatality in October the other patients in the hospital for thoracoplasty were discharged without operation.

The number of thoracoplasties performed in 1936 and 1937 was limited only by the beds available. The diminution in the number of these operations

per year, during 1938, 1939, and 1940, has been the direct result of the building of operating rooms by the state hospitals for tuberculosis\* and the shifting of our work more to intrathoracic tumors, pneumonectomies, and lobectomies, which are not included in this chart but in the group of miscellaneous operations (Chart 10).

#### THORACOPLASTIES, SECOND AND SUBSEQUENT STAGES†—CHART 5

These operations are placed in a separate chart as potentially infected since a reopened recent operative wound has two sources of infection which do not exist in the primary incision. The first of these is that the few organisms gaining entrance to the wound during the previous operation may find a harbor about a catgut suture, or in a collection of fluid in a dead space, multiply, but not give evidence of suppuration, and be present in much larger numbers to inoculate the second operative wound when fresh tissues are laid open. The second is that the organisms present in the deeper layers of the skin (hair follicles and sebaceous glands) may have grown along the skin sutures of the first closure which act as foreign bodies and form cleavage planes through the tissues. If the sutures are tied tightly, they constrict the blood supply and may cause necrosis, but under any condition diminish the resistance of the tissues to invasion by the organisms which are always present in the skin. Occasionally, if the sutures are left in for a relatively long period, a droplet of pus may be produced around one or more of them and present at the point where the suture pierces the skin—the well known stitch abscess. These have nothing to do with an operating room infection and, as already noted, are omitted from this statistical study both for the radiated and nonradiated operations. Certainly, in the case of stitch abscesses and, undoubtedly, about many sutures where there is no gross evidence of pus, there must be a growth of the skin organisms. When the incision is reopened 14–20 days after the preceding operation, and six to 15 days after the sutures have been removed, the scalpel must, in certain cases, pass through clusters of these organisms of relatively low virulence which are still viable. As a result, a low grade infection may result. In our cases, such an infection was usually restricted to the subcutaneous fat or to a collection of fluid in the wound. We feel that this latter explanation accounts for most of the infections in this group of reopened thoracoplasty wounds where radiation was used and for at least a part of the infections in this group where radiation was not used.

It has been observed also that where radiation was not used the infections

\* See note under Thoracoplasties, Second and Subsequent Stages for the experience of Doctor Monroe at one of these hospitals.

† Since this chart was originally designated to include all potentially infected thoracoplasties, one first-stage thoracoplasty—grossly contaminated by a considerable quantity of germ-laden perspiration during the operation—is included, and accounts for one of the two operative wounds classed as severely infected when radiation was used in 1936 (Case 3, Reference 9).

# INFECTED OPERATIVE WOUNDS

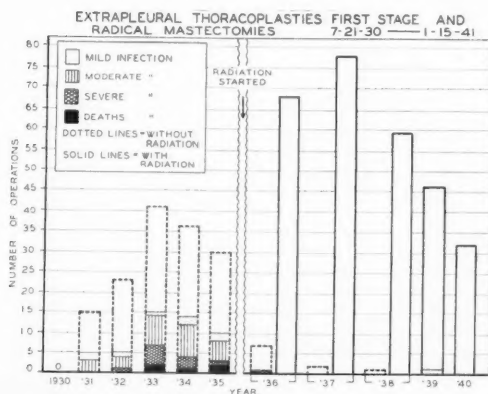


CHART 4.—Note the high infection rate before radiation was instituted, with only one *questionable mild infection\** in a much larger series of similar operations where radiation was used.

The lack of growth of this service in 1934 and 1935 was caused by the refusal of the staff to perform these operations during much of the year because of the "fear of infection." The rapid growth in 1936 and 1937 resulted from the removal of this fear by air sterilization and was limited only by the beds available for such cases. The drop in 1938-1940 resulted from the opening of surgical services at the State hospitals from which most of our patients had been referred. For a more careful analysis and for the experience of Doctor Monroe in reducing the infection rate for thoracoplasties at one of the State hospitals from 22.7 per cent to 1.09 per cent by the introduction of ultraviolet radiation for air sterilization see the text under Thoracoplasties, First Stage and Second and Subsequent Stages.

\* The "mild infection" in 1939 was thought by the operator to be only an hematoma, and drainage ceased within two days. Cultures, however, revealed both the *Staphylococcus aureus* and *albus*. Excision of an enlarged lymph node during the course of an apicolysis would, at least, have to be considered as a possible source of the infection if such existed. The organisms obtained by culture may have been from contamination with skin organisms at the time the culture was taken (for abstract see Case 6, Reference 7).

in reopened thoracoplasty wounds were less numerous, less severe, and less likely to be fatal than the infections occurring in the primary thoracoplasty incisions<sup>9</sup> (compare Charts 4 and 5). To us, the most logical explanation of this seemed to be that the patient, following the first operation, developed a certain amount of immunity, as is known to occur in the peritoneal cavity following multiple celiotomies for intestinal surgery. Even in these reopened, potentially infected wounds, with the introduction of bactericidal radiation the percentage which became infected was reduced from 23.4 to 6.4.

The effects of the fear of infection in extrapleural thoracoplasties on the growth of the service, during 1933, 1934, and 1935, are illustrated in this chart as in Chart 4. The drop, during and since 1938, followed the opening of operating rooms at the State Hospitals for Tuberculosis.

The experience of Dr. Clement R. Monroe<sup>10</sup> with infections at the State Sanatorium, Sanatorium, N. C., since opening their operating room, was given in a recent personal communication as follows:

"Before installing ultraviolet radiation at the State Sanatorium, we performed 75 thoracoplasty stages, with 17 severe infections. Since this installation we have performed 92 such operations, with the following results from the standpoint of infection:

- Severe infection—1—following *second-stage operation*.
- Stitch abscess—3—following *second-stage operation*.
- Stitch abscess—1—following *third-stage operation*.

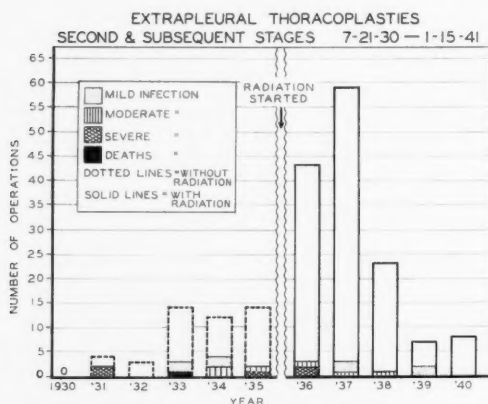


CHART 5.—Reopened wounds have a potential source of infection from organisms already present in the wound. These may have gained entrance at the preceding exposure or may have grown down along the skin sutures. Under either condition, having increased in number they may contaminate the tissues exposed at the subsequent operation sufficiently to cause gross suppuration. In our opinion, the few infections in these reopened wounds where radiation was used may be explained on this basis. For explanation of the few operations in 1934 and 1935, the great increase in 1936 and 1937, and the few since 1938, see the legend to Chart 4. See text for more complete analysis.

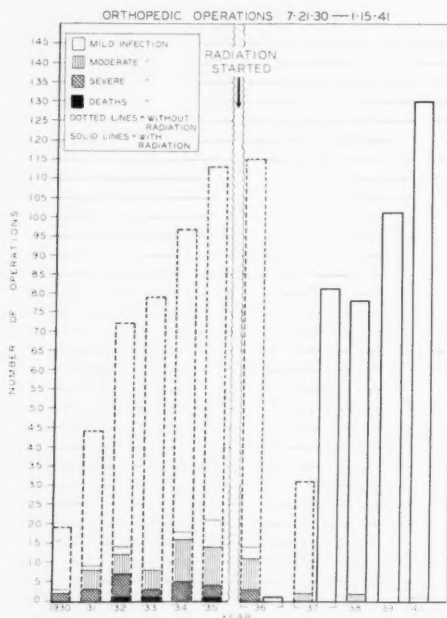


CHART 6.—The improvement in the infection rate in orthopedic operative wounds occurred in 1937 simultaneously with the adoption by this service of radiation for their larger operative wounds.\* Compare with other charts, in all of which the improvement in the infection rate varied as to time but was definitely correlated with the institution of radiation. See text for more complete analysis.

The mild infection (?) in 1940 was recorded, since six days following bilateral operations for hallux valgus what was described as "pus" was expressed from the wound on the right foot. Cultures failed to reveal any growth of organisms and the wound was described as "healing under compresses" without complications.

\*The two infections charted as moderate in 1938 were as follows:

- (1) One patient with a comminuted fracture of the patella, syphilis, and delirium tremens, walked around on the second and third days after an open reduction and developed an hematrosis. The fluid, on evacuation, contained the *Staphylococcus aureus*. The wound continued to drain and the patient developed an osteomyelitis of the patella.
- (2) Another patient with a triple arthrodesis for flaccid talipes equinovarus developed a large area of skin slough with a mixed infection (*Beta* hemolytic streptococcus and hemolytic staphylococcus aureus) in the wound. We cannot state whether or not this would have developed had there been adequate blood supply to the flaps.

"... We not only have many less infections but the postoperative courses are much better in all respects. I have now reached the point where I think I would hesitate a long time before undertaking a thoracoplasty in an operating room not equipped with ultraviolet radiation."

ORTHOPEDICS—CHART 6

Since sterilization of the air in the operating room was undertaken as an experimental project by one of us, and at first only one operating room was available, it was not used by the orthopedists, except for one case, until 1937, and then only for their larger procedures. The improvement with its use in these cases was so striking that, by 1938, it was used by them for most of their clean operations.

The year 1937 offers a striking illustration of the reduction in the infection rate in the nonradiated operations brought about by a selection of cases so that the operations more likely to become infected, were performed with bactericidal radiation. Whereas formerly the infections in clean orthopedic wounds ranged from 10–20 per cent (average 16.5 per cent) for different years, during this year only 6 per cent of these nonradiated clean operative wounds became infected and, then, the infections were of only moderate severity.

The large number of orthopedic operations in this report results from the high percentage of clean operations on this service, and the inclusion of many operations of smaller magnitude, such as excision of a semilunar cartilage or even an operation for hallux valgus. The percentage of infections in the larger arthroplasties alone was, therefore, higher than the infection rate for the entire group as shown by Chart 6.

The drop in the number of clean operations on this service, beginning in the fall of 1937 and 1938, was due to changes in personnel.

NEUROSURGERY—CHART 7

Chart 7 gives a striking illustration of the fact that in these patients, when an operative wound becomes infected, it is more likely than in any other type of operation to be fatal. This is particularly true for infections with some of the less virulent organisms which in the usual wound would produce only a mild reaction but in neurosurgery may cause a fatal meningitis (Chart 3). All these patients who died of infected wounds following clean operations developed a meningitis, two of them with the *Staphylococcus albus*. Chart 7, along with the others, illustrates, clearly, that the infection rate changed little during 1936 and subsequent years, except insofar as it was influenced by bactericidal radiation.

The fear of infection also limited the growth of this service during 1933, 1934, and 1935. As an example, during this period open operations upon patients suffering with trifacial neuralgia were virtually abandoned in favor of alcohol injections. The small percentage of neurosurgical patients operated upon with radiation during 1936 was the result of a shortage of suitably



equipped operating room space, and the difficulty encountered in working out for the operator an adequate protection which still permitted the use of a head

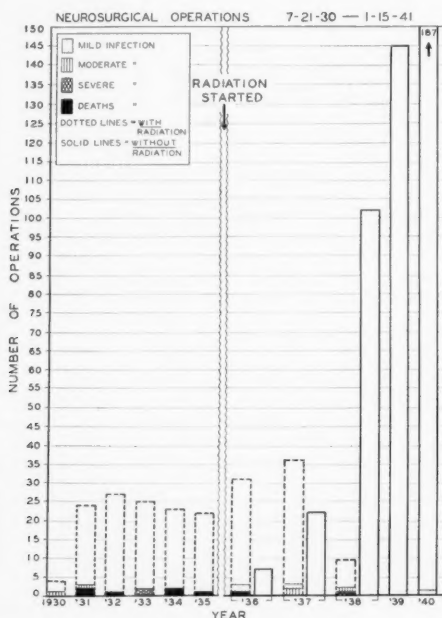


CHART 7.—Air sterilization was not adopted for all clean neurosurgical operations until early in 1938 for reasons as explained in the text. Infections have been practically eliminated\* where radiation was used. This chart also illustrates the lack of growth of the service during 1933, 1934, and 1935 resulting from the "fear of infection" as noted in the legends for Charts 4 and 5.

See text for more complete analysis.

\* The patient recorded as having a mild infection in 1940, developed two stitch abscesses four days following a cerebellar operation. No culture was made. On the seventeenth postoperative day, two small collections of pus were evacuated from the incision at the site of the stitch abscesses and cultures showed the hemolytic staphylococcus aureus. The wound had been closed with buried and skin sutures of silk. A spinal fluid fistula later opened at the site of the stitch abscesses. The patient died on the forty-fifth postoperative day as a result of the continuation of the tumor growth with an hemorrhage into the tumor. This infection was not classed as a stitch abscess because of the subsequent evacuation of pus. However, the organisms may have entered about the skin sutures and have been harbored about the buried silk sutures.

(During this same year a child with "morcellation of the skull" for oxycephaly, twice pulled off her dressings, fingered the wound, developed a skin slough from the tension, which was so great that the wound could scarcely be closed, and subsequently had an infection with the nonhemolytic staphylococcus aureus. Both the operator and I considered this infection to be secondary to the skin slough and subsequent contamination, so it was omitted from the chart but is mentioned here for completeness.)

lamp. During 1937, an increasing percentage of these operations were performed with radiation until September, when a change in personnel again raised the difficulties of an individual adjusting his operating technic, with the use of a head lamp, to adequate protection of himself. At this time, radiation was abandoned completely until early in 1938, with the resultant infections as shown in the chart for 1937 and 1938. Since early in 1938, radiation has been used for all large clean neurosurgical operations.

#### HERNIORRHAPHIES—CHART 8

The infections in hernia wounds without radiation were usually mild or moderate but are of serious import since they predispose to a recurrence.

## INFECTED OPERATIVE WOUNDS

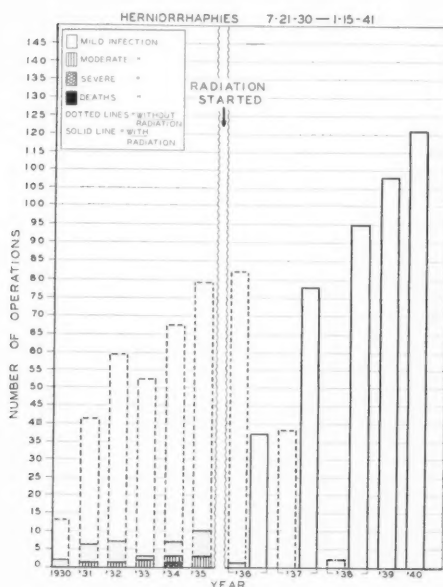


CHART 8.—Infections in hernia wounds were never severe or frequent enough to interfere with the growth of the service, but did cause the temporary abandonment of the "silk technic." After the institution of radiation, silk was again used in all clean hernia operations. The absence of infection and the improved healing brought about by a diminution in the wound contamination and the use of less irritating suture material has undoubtedly resulted in a diminution in the percentage of recurrences.\*

\* The statistics on infections in hernia wounds were obtained from Dr. William F. Hollister, who is making a survey of the postoperative results. This survey has not been completed, but it seems safe to prophesy that since the institution of bactericidal radiation and the return to silk technic, the percentage of recurrence after comparable periods of time will be greatly reduced.

## THYROIDECTOMIES—CHART 9

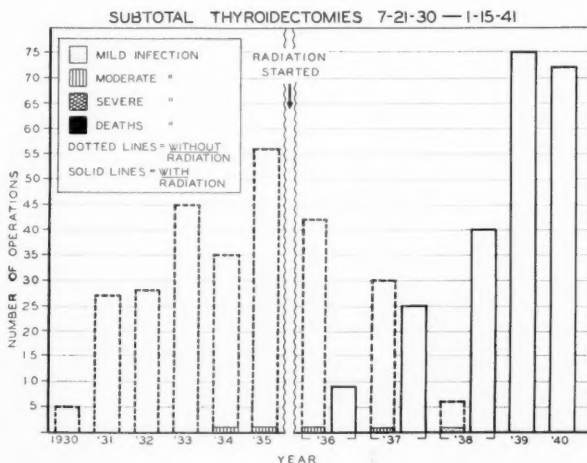


CHART 9.—Before beginning the use of radiation, infections in our thyroid wounds were rare and no infection was severe or fatal so there was no curtailment in the growth of this service because of "fear of infection" and silk was never abandoned. Air sterilization, however, has produced an appreciable improvement by the elimination of the occasional moderate infection that had occurred when the air was not sterilized.

This analysis should be interpreted with the following facts in mind:

(1) After 1936, silk was again used (it had been abandoned previously because of the recurring infections) for all hernia operations and this, of course, had its effect in securing improved wound healing.

(2) The skin in the inguinal region, as contrasted to most other areas of the body, has a much larger number of bacteria present toward the end of an operation, particularly when the patient is perspiring freely.

(3) Some of the herniae were large, as the incisional, and umbilical, while others, particularly the inguinal herniae in children, were small.

(4) With the institution of bactericidal radiation for the larger hernia operations, during 1936 and 1937, infections were almost eliminated. (It should be emphasized again that all feasible precautions were already in use to protect the open wound from the skin organism.)

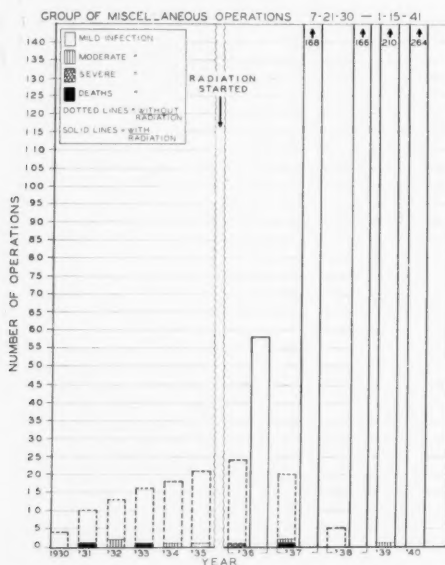


CHART 10.—This chart includes all operations performed with radiation and not included in Charts 4-9. It is given in order to make a complete presentation of our operative experience with the use of air sterilization. See text for more complete analysis.

#### MISCELLANEOUS OPERATIONS—CHART 10

Beginning shortly after the installation of the first radiation unit an increasing number of miscellaneous operations (Chart 10) not included in Charts 4-9, inclusive, have been performed in such a field of sterile air. They include a wide variety of operations in general—thoracic, plastic, and urologic surgery—and this chart serves, primarily, to complete the presentation of the total number of operations performed in a field of ultraviolet radiations. It also shows the improvement in this heterogeneous group of operations brought about by the use of air sterilization, even though their diverse types make comparisons somewhat less valuable.

The cases without radiation that were analyzed include only splenectomies, certain other celiotomies where the hollow viscera were not opened, nerve sutures, excision of benign breast tumors, and certain other tumors over the body. Also in this group are the remaining three deaths from infections listed on Chart 3, and not included in the operations shown on Charts 4-9, inclusive. Other types of these miscellaneous operations performed without radiation were not analyzed because there was not a sufficient number of any one type to give statistics which could be evaluated or compared.

The radiated group in this chart is more diverse, since every operation performed in a field of bactericidal radiation and not included in one of the other charts is listed here. Slightly less than 200 of these were potentially infected at the time of the operation. All operations with radiation are included in the columns indicating the totals, but every potentially infected case both with and without radiation was ruled out in the analysis for infections in clean operations as indicated by the shaded area. After eliminating these potentially infected operations, there were between 600 and 700 miscellaneous clean operations performed in a field of ultraviolet radiation, with only one infection.

This infection with the hemolytic staphylococcus aureus followed a four-hour operation for removal of a cystic hygroma of the neck, during the course of which the submaxillary gland was cut across. It may have resulted from cutting across the salivary gland, from lymphatic drainage from the mouth or respiratory passages, from skin contaminants, or may have originated from contaminants reaching the wound from outside the body, such as from the air or from some other unexplained source.

#### INFECTING ORGANISMS

Ninety-one per cent of the organisms causing the infections reported in this survey both in the fatal and nonfatal cases, with and without radiation, were staphylococci, while 83 per cent of all offending organisms were hemolytic or nonhemolytic staphylococcus aureus (Table I). Many of the organisms reported as *Staphylococcus aureus* were undoubtedly hemolytic, as the laboratory did not always report on hemolysis. In general, the more severe infections were caused by the hemolytic staphylococcus aureus or by a combination of a hemolytic streptococcus with the *Staphylococcus aureus* or colon bacillus, with the exception that in certain brain operations, organisms of relatively low virulence at times produced a fatal meningitis (Chart 3).

Of the 142 positively identified organisms, 127 were from 207\* infected wounds in the 1,735 large clean operations performed without radiation, and eight were from the nine infected wounds among the 140 reopened thoracoplasty wounds where radiation was used. Only seven were from six mild

\* Many orthopedic patients were discharged in a plaster encasement, without a culture having been taken, and the infection was diagnosed without a culture from the draining wound described in the follow-up clinic; in certain other cases a culture was taken but the report was not recorded, while in some mild or moderate infections there was no record of a culture having been taken.

or moderately infected wounds (two having mixed infections, and one having no growth) out of a total of 2,463+ clean primary incisions (including 283 first-stage thoracoplasties and radical mastectomies) where radiation was used (Charts 2-10 and Table I), as follows:

- (1) First-stage thoracoplasty, with excision of an enlarged lymph node during mobilization of the apex (Chart 4).
- (2) Triple arthrodesis of the ankle, with a large slough of the skin flaps (Chart 6).
- (3) Open reduction—comminuted fracture patella—where rest was not obtained (Chart 6).
- (4) Cerebellar exploration—probably started as a stitch abscess (Chart 7).
- (5) Excision of hygroma neck, with cutting across lymphatics and submaxillary gland (Chart 10).

Out of this total of 142 positively identified organisms in wounds, either in pure or mixed culture, the *Beta* hemolytic streptococcus was present only seven times, or 5 per cent of the total (Table I). Six of these seven were mixed infections (with the hemolytic staphylococcus aureus in two, the *Staphylococcus aureus* [no note as to hemolysis] in three, and the colon bacillus in one, the only pure culture being from an hernia, with a mild infection. Four of the seven wounds infected with hemolytic streptococci were on the Orthopedic Division,\* and three of the four patients so infected died as a result. The only death from a streptococcal wound infection, other than on the Orthopedic Service, was from peritonitis following biopsy of a retro-peritoneal lymph node during a celiotomy for an inoperable carcinoma of the stomach. This infection, in a debilitated patient (Chart 3—March 21, 1931), may have followed cutting across infected lymphatics.

Thus, four, or 21 per cent, of the 19 patients who died of an "unexplained" operative or postoperative infection (Chart 3) showed the *Beta* hemolytic streptococcus in their wound, but in none of the four was it present in pure culture. However, the two of these four patients with a proven septicemia did show the *Beta* hemolytic streptococcus in pure culture in their blood. Thus, even though this organism was present, usually as a mixed infection, in only 5 per cent of the total infections, it was present and played an important rôle in 21 per cent of the deaths from infection. We are unable to make any statement as to whether or not the combination of organisms increased the severity of these streptococcal infections, but it seems quite likely that it did.

Undoubtedly, when the *Beta* hemolytic streptococcus is a common respiratory tract contaminant it will assume a rôle of increasing importance, insofar as wound infections are concerned. This is illustrated clearly in the report, of Walker,<sup>11</sup> from a teaching hospital in Boston, where at one time during

\*This suggests the possibility of a carrier being present on that service.



the winter months the postoperative infection rate was as high as 42 per cent, with an exacerbation of streptococcal wound infections simultaneously with an increase in the streptococcal throat infections.

In our experience, also, at certain periods severe operative infections are far more prevalent than at others, as illustrated by the months of November, December, and January, 1933-1934 (Chart 3). During this time, there were six deaths as a result of clean wounds becoming infected, all with the *Staphylococcus aureus* (hemolytic in four, but with no note as to hemolysis in two), but with one patient's wound also showing the *Beta* hemolytic streptococcus. Cultures revealed that a number of the personnel were persistent carriers of the hemolytic staphylococcus aureus in their nose and throat, and, at one time, approximately 80 per cent of the general population and of the operating room personnel were either transient or persistent carriers of the hemolytic or nonhemolytic staphylococcus aureus in their respiratory passages. During other years, the percentage of positive cultures of these organisms from the nose and throat has remained far below this level.

Of the 19 patients dying from infection in a clean wound, in none of which radiation was used (Chart 3), only five (four with brain operations and one with an orthopedic operation) failed to show the *Staphylococcus aureus* in their wound, and one of these showed, on the smear, gram-positive cocci in clumps—probably staphylococci—but the culture was overgrown with *B. proteus* and this organism was not positively identified. Eleven of the patients who died (including three of the seven patients dying of meningitis following a brain operation) had their wound infected with the *Staphylococcus aureus* in pure culture. In nine of these, it was definitely stated that the organism was hemolytic, while in two there was no note as to hemolysis (Chart 3). In neurosurgery, death from meningitis may be caused by less virulent organisms, which in the usual wound would at most cause only a trivial or moderate infection. This is illustrated by the four deaths from meningitis, caused by the *Staphylococcus albus* in two cases, a gram-positive diplococcus in one case, and by an unidentified gram-positive coccus in clumps in one case (Chart 3). All other deaths from infection were caused by the *Staphylococcus aureus*, usually hemolytic, or the hemolytic streptococcus, or a combination of organisms, in which one or both of these played a part.

Where radiation was used, there has been no severe or fatal "unexplained" wound infection in any clean primary incision or reopened wound. The six infections, or 0.24 per cent, some of questionable origin, that occurred were caused by *Staphylococcus aureus* or *albus* in all cases, except one orthopedic operation where there was a mixed infection with the *Beta* hemolytic streptococcus and hemolytic staphylococcus aureus. The latter infection may have occurred in the operating room but it may not have developed had not there been a large skin slough (Chart 6). It is interesting to note that this is the only orthopedic patient in this report infected with this combination of organisms who did not die as a result of the infection.

TABLE I  
ORGANISMS CAUSING INFECTION IN CLEAN WOUNDS (7/21/30-1/15/41)

Organism	Without Radiation		With Radiation		
	All Wounds	Wounds with Fatal Infection	Primary Incision	Reopened Wounds	Deaths from Infection
Hem. staph. aureus	54	9	2	3	0
Staph. aureus*	44	2	2	3	0
(Staph. aureus)					
(B. hem. strep.)	3	3	0	0	0
(Hem. staph. aureus)					
(B. hem. strep.)	1	0	1	0	0
Staph. albus	9	2	1	2	0
B. hem. strep.	1	0	0	0	0
(B. hem. strep.)					
(B. coli communior)	1	1	0	0	0
Colon bacillus	3	0	0	0	0
Proteus overgrowth	2	1	0	0	0
B. subtilis	2	0	0	0	0
B. pyocyaneus	1	0	0	0	0
Gram-pos. diplococci	1	1	0	0	0
Total organisms	127	23	7	8	0

\* This group contains all organisms where there was no note as to hemolysis. Since the cultures were made by interns rotating through the laboratory, and they, at times, did not differentiate between hemolytic and nonhemolytic staphylococci, undoubtedly a number of these organisms were hemolytic.

Ninety-one per cent of all positive cultures showed a staphylococcus, with the *Staphylococcus aureus* (hemolytic or nonhemolytic) in 83 per cent. Five of the wounds (3.6 per cent of the total with positive culture) showing *Staphylococcus aureus* also contained the *Beta* hemolytic streptococcus. The latter organism was present only seven times (5.1 per cent of all infected wounds), on only one occasion in pure culture (a mild infection in an inguinal hernia), while the mixed infections showed, in addition, staphylococci in five, and colon bacilli in one. Four of these six mixed infections resulted in the death of the patient (Chart 3). With the exception of brain operations where an organism of relatively low virulence may cause death from meningitis, all fatal infections were caused by the hemolytic staphylococcus aureus or the *Beta* hemolytic streptococcus either singly or as part of a mixed infection. A combination of these two organisms seemed to be particularly virulent (Chart 3).

## SUMMARY AND CONCLUSIONS

(1) In evaluating air sterilization as an addition to "aseptic operating room technic," selected groups of large clean operations (all thoracoplasties, radical mastectomies, herniorrhaphies, thyroidectomies, orthopedic, and neurosurgical operations), some of each group performed with and others without radiation, as given in the charts, and covering a period of ten and one-half years, were analyzed for unexplained infections.

The operations analyzed can be divided into two groups:

- (I) 1,313 out of a total of 15,674 performed before radiation was instituted—a period of five and one-half years, and

- (II) 3,272 (469 without radiation and 2,803 with radiation) out of a total of 30,695, performed after radiation was instituted—a period of five years.

As a further check on the value of bactericidal radiation the records of all patients dying following any type of operation (approximately 700 were analyzed to determine the number of deaths from "unexplained" infections in clean wounds). Out of the first group of 15,674 operations, before radiation was instituted, there were 17 deaths from "unexplained" infections (Charts 1 and 3), while out of the second group of 30,695 operations, after radiation was instituted, there have been only two deaths from "unexplained" infection where radiation was not used and no such death where radiation was used (Charts 1 and 3). During this last period most of the large wounds likely to develop a severe infection have been protected from air contaminants during operation by bactericidal radiation.

(3) The air in the operating room is contaminated by the occupants who carry pathogenic organisms in their noses and throats.<sup>13</sup>

(4) The generally accepted operating room mask will prevent massive droplet infection, but will not prevent the nose and throat contaminants from being given off into the air in finer particles.

(5) Fatal "unexplained" wound infections in the Duke Hospital have occurred only during the months when the air contamination and respiratory tract infections were likely to be high (Chart 3).

(6) Severe "unexplained" operating room infections may reach epidemic proportions at rare intervals (Chart 3).

(7) The degree of air contamination can be reduced by supplying large quantities of clean air which is not recirculated, or by sterilizing recirculated air in the ducts, but recontamination of the air by the occupants of the room prevents a reduction in the bacterial level by these measures to a point adequate for the prevention of wound infection.

(8) After a most detailed analysis of the conditions in our operating rooms, covering a period of several years, we were forced to the conclusion that the pathogenic bacteria, given off from the respiratory passages of the occupants, and floating in the air, constituted the greatest hazard of infection in a clean wound in the modern well-run operating room.

(9) As an experimental project to prove or disprove the conclusions given in the preceding paragraph (8), we adopted air sterilization by ultraviolet radiation (over 85 per cent at  $2537\text{\AA}$ ) of an intensity throughout the entire room adequate to reduce the sedimenting viable bacteria at the operative site (including the sterile supplies) to 1-2 colonies per Petri dish, per hour of exposure.

Although many things may be done to reduce the air contamination, we have as yet found no method that is as adequate or as simple as continuous exposure of the air to this bactericidal radiation.

*Attention must be kept centered on the importance of air contamination*

in the operating room and not diverted to the particular method of controlling it.

(10) Sterilization of the air by radiation resulted in the following reduction in the "unexplained" infections (Table II):

TABLE II

	Without Radiation	With Radiation
Thoracoplasties, first-stage; and radical mastectomies	32%	to 0.35%
Orthopedic operations	16.5%	to 0.74%
Neurosurgical operations	9%	to 0.22%
Herniorrhaphies	8.3%	to 0.00%
Partial thyroidectomies	1.8%	to 0.00%

(11) The death rate from "unexplained" infections in these large clean operations reported, was reduced from 1.07 per cent in 1,735 operations performed with the generally accepted methods of protecting the wounds during operation from nose and throat contaminants, to zero per cent in 2,463+ operations performed with the wound protected during operation by sterilization of the air with ultraviolet radiation.

(12) Reopened wounds are more likely than primary incisions to become infected from sources other than the air.

(13) In the North Carolina Sanatorium, at Sanatorium, N. C., the percentage of thoracoplasty wounds (all stages) having severe infections was reduced from 22.7 per cent in 75 consecutive operations without radiation to 1.09 per cent for the next 92 operations which were performed with bactericidal radiation. The only operating room infection in the latter group was in a wound reopened for the second stage (compare with Charts 4 and 5).

(14) The pathogenic bacteria most commonly encountered in this ten and one-half-year period of study covering wound infections, air contamination, and the nose and throat flora, have been *Staphylococcus aureus*, both hemolytic and nonhemolytic (Chart 3 and Table I).

Hemolytic streptococci, while rarely encountered in this analysis (5 per cent of the total identified organisms obtained from wounds), have usually occurred in combination with other organisms, predominantly *Staphylococcus aureus* (Chart 3 and Table I), and have caused the death of 57 per cent (four out of seven) of the patients so infected. Even though infections with the hemolytic streptococcus in our experience have been rare, under conditions of widespread nose and throat contamination with this organism, it can become a major threat in any operating room if air transportation of bacteria is ignored.

(15) In wounds protected from air contaminants during operation by sterilization of the air with ultraviolet radiation, any type of "unexplained" infection in a clean wound was extremely rare and never severe. This indicates that the organisms were present in smaller numbers, were attenuated or less virulent, gained access to only a localized part of the wound, or that

the wound itself had an increased resistance to the infection (Charts 3-10 and Table I).

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## BOOK REVIEWS

TEXTBOOK OF SURGERY. By JOHN HOMANS, M.D., Fifth Edition. Springfield, Ill.: Charles C. Thomas Co., 1940.

IN THE PREFACE to the First Edition of Homan's Surgery, the author credits Dr. Harvey Cushing with inspiring him to record and amplify lectures then given by members of the Surgical Department of the Harvard Medical School, and to put into writing within a single volume the history, the fundamentals, and something of the practice of surgery. The immediate success of his first edition was evidence that he accomplished these aims, and a second edition followed within a year. The present volume completes the fifth, published in less than nine years. This is a record that should be enough to satisfy even the present generation of undergraduate medical students, and it certainly is an unusual achievement for an author at the present time.

To attempt to review in detail the text of this last edition would be like "painting the lily." As in all former editions, it makes delightful reading, and to the reviewer, no higher compliment could be received than a recent statement of a medical student: "It reads like a novel."

WALTER ESTELL LEE, M.D.

PUBLICATIONS FROM THE DIVISION OF SURGERY OF THE NORTHWESTERN UNIVERSITY MEDICAL SCHOOL. Chicago: 1940.

THE PUBLICATIONS during 1939 of the Division of Surgery of the Northwestern University Medical School have been collected and published as Volume 6.

These papers have all appeared in various medical and surgical journals during the year, and as they are not indexed in this volume, nor are they arranged in such a way as to facilitate their use for reference, it is evidently the intention of the editors that the papers will be consulted and referred to as indexed in the Index Medicus and the Quarterly Index.

The 44 papers cover many subjects, including Technic, Pre- and Postoperative Care, Water and Electrolyte Balance, Chemotherapy, Diseases, Congenital Anomalies, Trauma, Malignancies of Special Organs, and many Systems, and they represent productive effort of which the Medical School has reason to be proud.

WALTER ESTELL LEE, M.D.

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East Washington Square, Philadelphia, Pa.